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Organized by :

Thai Society of Clinical Oncology

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WELCOME MESSAGE

เรียน สมาชิกมะเร็งวิทยาสมาคมแห่งประเทศไทย และเพื่อนร่วมวิชาชีพ

ในนามของมะเร็งวิทยาสมาคมแห่งประเทศไทย ขอเรียนเชิญทุกท่านเข้าร่วมงานประชุมวิชาการ Best of ASCO® Bangkok 2024 ที่จะจัดขึ้นในรูปแบบ onsite ในวันที่ 23-24 สิงหาคม พ.ศ. 2567ณ โรงแรมอีสติน แกรนด์ พญาไท โดย Best of ASCO® Bangkok เป็นงานประชุมวิชาการที่มะเร็งวิทยาสมาคมแห่งประเทศไทยได้รับลิขสิทธิ์จาก American Society of Clinical Oncology (ASCO) โดยมีวัตถุประสงค์เพื่อนำเสนองานวิจัยที่สำคัญและโดดเด่นในงานประชุมประจำปีของ ASCO โดยงานวิจัยที่นำเสนอและอภิปรายเป็นงานที่น่าจะมีผลเปลี่ยนแปลงในการดูแลรักษาผู้ป่วยและสามารถนำไปใช้ได้ในเวชปฏิบัติ สำหรับงานประชุมในปีนี้มีการเปลี่ยนแปลงจากปีก่อนๆ คือ การใช้ภาษาไทยเป็นภาษาหลักในงานประชุม เพื่อให้สมาชิกได้รับประโยชน์สูงสุด

ในการนี้ จึงขอเชิญชวนสมาชิกและเพื่อนร่วมวิชาชีพที่สนใจลงทะเบียนเข้าร่วมงานประชุมวิชาการ Best of ASCO® Bangkok 2024 หวังเป็นอย่างยิ่งว่าจะได้พบกับทุกท่านใน Best of ASCO® Bangkok 2024

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นายกมะเร็งวิทยาสมาคมแห่งประเทศไทย

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PROGRAM

Best of ASCO Bangkok 2024
(Day 1: 23 August 2024)

Time	Title	Presenter	Moderator
08.00-09.00	New Treatment Options for Patients with Oncogene Addicted- Non-Small Cell Lung Cancer	SUNATEE SA-NGUANSAI, M.D. Assistant Professor SIRIWIMON SAICHAEMCHAN, M.D. LUCKSAMON THAMLIKITKUL, M.D., Ph.D.	*Associate Professor CHANIDA VINAYANUWATTIKUN, MD., PH.D.*
09.00-09.10	Opening and welcome message	Associate Professor CHARUWAN AKEWANLOP, M.D. Assistant Professor SUEBPONG TANASANVIMON, M.D.	*President, Thai Society of Clinical Oncology* *Scientific Chairman, Thai Society of Clinical Oncology*
	Head and Neck Cancers (Thai)		
09.15-09.25	Adjuvant PD-1 blockade with camrelizumab in high-risk locoregionally advanced nasopharyngeal carcinoma (DIPPER): A multicenter, open-label, phase 3, randomized controlled trial.	Associate Professor ARUNEE DECHAPHUNKUL, M.D.	*Associate Professor CHANYOOT BANDIDWATTANAWONG, M.D.*
09.25-09.35	Phase III randomized trial of intensity-modulated proton therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for the treatment of head and neck oropharyngeal carcinoma (OPC).	Adjunct Assistant Professor ANUSSARA PRAYONGRAT, M.D., Ph.D. (RT Chula)	
09.35-09.50	Discussion / Q&A	Associate Professor NUTTAPONG NGAMPHAIBOON, M.D.	
09.50-10.10	**Exhibition**		
10.10-10.55	**Strategic Sequencing: Enhancing Outcomes in Advanced HCC Treatment**	**Professor Toh Han Chong National Cancer Centre Singapore**	***Assistant Professor SUEBPONG TANASANVIMON, M.D.***
	Hepatocellular carcinoma (English)		
10.55-11.05	Nivolumab (NIVO) plus ipilimumab (IPI) vs lenvatinib (LEN) or sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC): first results from CheckMate 9DW.	Associate Professor KOSIN WIRASORN, M.D.	*Assistant Professor SUEBPONG TANASANVIMON, M.D.*
11.05-11.15	Discussion / Q&A	**Professor Toh Han Chong**	

Time	Title	Presenter	Moderator
	Gastrointestinal Cancer: Colorectal (Thai)		
11.20-11.30	Chemotherapy and liver transplantation versus chemotherapy alone in patients with definitively unresectable colorectal liver metastases: A prospective multicentric randomized trial (TRANSMET).	*PARICHAT PHONGTHAI, M.D.*	*Associate Professor EKAPHOP SIRACHAINAN, M.D.*
11.30-11.40	Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer: Overall survival and updated 5-year results from the randomized DYNAMIC trial.	*NUSSARA PAKVISAL, M.D.*	
11.40-11.55	Discussion / Q&A	*Assistant Professor SUEBPONG TANASANVIMON, M.D.*	
11.55-12.05	Nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) as first-line (1L) treatment for microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Expanded efficacy analysis from CheckMate 8HW.	*PANUNAT MUANGNOI, M.D.*	
12.05-12.15	Surgery versus thermal ablation for small-size colorectal liver metastases (COLLISION): An international, multicenter, phase III randomized controlled trial.	*NATTAYA TEEYAPUN, M.D.*	
12.15-12.30	Discussion / Q&A	*Associate Professor KRITTAYA KORPHAISARN, M.D.*	
12.35-13.20	**CLEAR the Way to Optimize Treatment Options for Patients with RCC**	***Associate Professor Ravindran Kanesvaran National Cancer Centre Singapore (on-line)***	***Assistant Professor PONGWUT DANCHAIVIJITR, M.D.***
13.20-13.40	**Exhibition**		
	Melanoma/Supportive Care (Thai)		
13.40-13.50	Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial.	*Assistant Professor JOMJIT CHANTHARASAMEE, M.D.*	*Associate Professor PATRAPIM SUNPAWERAVONG, M.D.*
13.50-14.00	Discussion / Q&A	*TOUCH ATIVITAVAS, M.D.*	
14.00-14.10	Comparative effectiveness trial of early palliative care delivered via telehealth versus in person among patients with advanced lung cancer.	*Assistant Professor CHAWALIT CHAYANGSU, M.D.*	
14.20-14.35	Discussion / Q&A	*PHICHAI CHANSRIWONG, M.D.*	

Time	Title	Presenter	Moderator
14.35-15.20	**The Evolving Treatment Landscape of Immunotherapy in Perioperative Early-Stage NSCLC**	***Mariano Provencio Pulla. MD, PhD Autonomous University of Madrid (on-line)***	***Assistant Professor PONGWUT DANCHAIVIJITR, M.D.***
15.20-15.40	**Exhibition**		
	Genitourinary cancer (English)		
15.40-15.50	Characterization of complete responders to nivolumab + gemcitabine-cisplatin vs gemcitabine-cisplatin alone and patients with lymph node–only metastatic urothelial carcinoma from the CheckMate 901 trial.	*NATTAYA POOVORAWAN, M.D.*	*Associate Professor CHARUWAN AKEWANLOP, M.D.*
15.50-16.00	Discussion / Q&A	***Associate Professor Peter H. O'Donnell***	
16.00-16.10	Effect of polygenic risk score for clinically significant prostate cancer in a screening program: The BARCODE 1 study results.	*Associate Professor JARIN CHINDAPRASIRT, M.D.*	
16.10-16.20	Discussion / Q&A	*Assistant Professor PONGWUT DANCHAIVIJITR, M.D.*	
16.20-17.05	**Evolving treatment landscape of locally advance and metastasis urothelial cancer**	***Associate Professor Peter H. O'Donnell The University of Chicago***	***Professor VIROTE SRIURANPONG, M.D., Ph.D.***

PROGRAM

Best of ASCO Bangkok 2024
(Day 2: 24 August 2024)

Time	Title	Presenter	Moderator
07.30-08.30	Systemic Thearpy in Breast Cancer: Current State of the Art and Future Horizons	*YOTSAWAJ RUNGLODVATANA, M.D.* *Assistant professor of Practice ARCHARA SUPAVAVEJ, M.D.* *PIYAWAN TIENCHAIANANDA, M.D.*	*Associate Professor NAPA PARINYANITIKUL, M.D.*
08.35-09.20	**Overcoming KRASG12C-mutated NSCLC: from clinical to practice**	***Associate Professor Ferdinandos Skoulidis*** ***The University of Texas MD Anderson Cancer Center***	***LUCKSAMON THAMLIKITKUL, M.D., Ph.D.***
	EGFR mutated NSCLC (English)		
09.20-09.30	Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study.	*Associate Professor CHANIDA VINAYANUWATTIKUN, MD., PH.D.*	*Professor VIROTE SRIURANPONG, M.D.,Ph.D.*
09.30-09.40	Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory EGFR-mutated, advanced non-small cell lung cancer (NSCLC): Primary results, including overall survival (OS), from the global, phase 3, randomized controlled PALOMA-3 trial.	*KUNLATIDA MANEENIL, M.D.*	
09.40-09.55	Discussion / Q&A	***Associate Professor Ferdinandos Skoulidis***	
09.55-10.15	**Exhibition**		
10.15-11.00	**ourney to the Stars: Manifesting the Effective ALK Treatment From Advanced to Early Stage Lung cancer**	***Professor Shirish M Gadgeel, MD***	***Associate Professor THAYANAN BAISAMUT, M.D.***
	SLCLC (English)		
11.00-11.10	ADRIATIC: durvalumab (D) as consolidation treatment (tx) for patients (pts) with limited-stage small-cell lung cancer (LS-SCLC).	*Assistant professor PIYADA SITTHIDEATPHAIBOON, M.D.*	*Professor VIROTE SRIURANPONG, M.D.,Ph.D.*

Time	Title	Presenter	Moderator
11.10-11.20	DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastasis.	*LUCKSAMON THAMLIKITKUL, M.D.,Ph.D.*	
11.20-11.35	Discussion / Q&A	***Professor Shirish M Gadgeel, MD***	
	KRAS G12C NSCLC and Mesothelioma (Thai)		
11.35-11.45	KRYSTAL-12: Phase 3 study of adagrasib versus docetaxel in patients with previously treated advanced/metastatic non-small cell lung cancer (NSCLC) harboring a KRASG12C mutation.	*Assistant Professor SIRIWIMON SAICHAEMCHAN, M.D.*	*Associate Professor BUSYAMAS CHEWASKULYONG, M.D.*
11.45-11.55	BEAT-meso: A randomized phase III study of bevacizumab (B) and standard chemotherapy (C) with or without atezolizumab (A), as first-line treatment (TX) for advanced pleural mesothelioma (PM)—Results from the ETOP 13-18 trial.	*APISADA SUTHEPWANON, M.D.*	
11.55-12.10	Discussion / Q&A	*Associate Professor THAYANAN BAISAMUT, M.D.*	
12.10-12.55	**Immunotherapy for advanced gastric cancer in real-life practice**	***Associate Professor Sung Hee Lim, MD, Samsung Medical Center***	***Assistant Professor SUEBPONG TANASANVIMON, M.D.***
12.55-13:15	**Exhibition**		
	Gastrointestinal Cancer: non-colorectal (Thai)		
13.15-13.25	Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (ESOPEC trial).	*Assistant Professor THATTHAN SUKSOMBOONCHAROEN, M.D.*	*Associate Professor CHAIYUT CHAROENTUM, M.D.*
13.25-13.35	NRG Oncology/RTOG 0848: Results after adjuvant chemotherapy +/- chemoradiation for patients with resected periampullary pancreatic adenocarcinoma (PA).	*Assistant Professor CHIRAWADEE SATHITRUANGSAK , M.D.*	
13.35-13.50	Discussion / Q&A	*Assistant Professor NAIYARAT PRASONGSOOK, M.D.*	
13.50-14.35	**Revolutionizing HER2+ Early Breast Cancer Treatment: Enhancing Patient**	***Associate Professor MATTEO LAMBERTINI the University of Genova – IRCCS Policlinico San Martino Hospital in Genova*** ***Assistant Professor Lt.Col. Naiyarat Prasongsok***	***Associate Professor CHARUWAN AKEWANLOP, M.D.***

Time	Title	Presenter	Moderator
	Advanced Breast Cancer (English)		
14.35-14.45	Abemaciclib plus fulvestrant vs fulvestrant alone for HR+, HER2- advanced breast cancer following progression on a prior CDK4/6 inhibitor plus endocrine therapy: Primary outcome of the phase 3 postMONARCH trial.	*PIYAWAN TIENCHAIANANDA, M.D.*	*Assistant Professor THITIYA DEJTHEVAPORN, M.D.*
14.45-14.55	Trastuzumab deruxtecan (T-DXd) vs physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06).	*Associate Professor NAPA PARINYANITIKUL, M.D.*	
14.55-15.10	Discussion / Q&A	***Associate Professor MATTEO LAMBERTINI***	
	Loco-regional Breast Cancer (Thai)		
15.10-15.20	A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.	*THANATE DAJSAKDIPON, M.D.*	*Assistant Professor AUMKHAE SOOKPRASERT, M.D.*
15.20-15.30	A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY Trial.	*Assistant Professor HATAIWAN RATANABUNJERDKUL, M.D.*	
15.30-15.45	Discussion / Q&A	*Associate Professor SUTHINEE ITHIMAKIN, M.D.*	
15.45	Closing remark		

ABSTRACTS

ABSTRACTS

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Adjuvant PD-1 blockade with camrelizumab in high-risk locoregionally advanced nasopharyngeal carcinoma (DIPPER): A multicenter, open-label, phase 3, randomized controlled trial.

Jun Ma, Ying Sun, Ye-Lin Liang, Xu Liu, Liangfang Shen, Weihan Hu, Guangyuan Hu, Fangyun Xie, Ying Huang, Guorong Zou, Ning Zhang, Chuanben Chen, Xiaozhong Chen, Xiaodong Zhu, Yawei Yuan, Kunyu Yang, Feng Jin, Shu-Bin Hong, Hongyun Zhao, Ji-Bin Li; Department of Radiation Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China; Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangzhou, Guangdong, China; Department of Radiation Oncology, Sun Yatsen University Cancer Center, Guangzhou, China; Xiangya Hospital of Central South University, Changsha, China; Department of Oncology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Department of Radiation Oncology,Sun Yat-sen University Cancer Centre, State Key Laboratory of Oncology in South China, Collaborative Innovation Centre for Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangzhou, China; Panyu Central Hospital, Guangzhou, China; First People's Hospital of Foshan City, Foshan, China; Fujian Medical University Cancer Hospital, Fuzhou, China; Zhejiang Cancer Hospital, Hangzhou, China; Guangxi Medical University Affiliated Tumor Hospital, Guilin, China; Affiliated Cancer Hospital and Institute of Guangzhou Medical University, Guangzhou, China; Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; Guizhou Cancer Hospital, Guiyang, China; Department of Endocrinology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; Department of Clinical Research, Sun Yat-sen University Cancer Center, Guangzhou, China; Clinical Trials Center, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Patients with high-risk locoregionally advanced nasopharyngeal carcinoma (NPC) often experience disease relapse even after receiving standard-of-care treatment, e.g. induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT). The benefit of PD-1 inhibitor as adjuvant treatment following IC+CCRT in locoregionally advanced NPC remains unclear.

Methods: Patients with high-risk locoregionally advanced NPC (T4N1M0 or T1-4N2-3M0) who have received gemcitabine and cisplatin (GP) IC and CCRT were recruited at 11 centers in China. They were randomly assigned (1:1) within 2 weeks after the last radiation dose to receive intravenous camrelizumab (200 mg once every 3 weeks for 12 cycles; Camrelizumab Arm) or observation (Standard-therapy Arm). The primary endpoint was event-free survival (EFS). It is estimated that approximately 442 patients would provide 80% power to detect a hazard ratio (HR) of 0.52 with a log-rank test at a two-sided a level of 0.05. Quality of life (QoL) was assessed by EORTC-C30.

Results: A total of 450 patients were randomly assigned to the Camrelizumab Arm (n=226) and the Standard-therapy Arm (n=224). After a median follow-up of 37 months (corresponding to 41 months when calculated from the start of standard therapy), the estimated 3-year EFS was 86.9% in the Camrelizumab Arm and 77.4% in the Standard-therapy Arm (intention-to-treat population; HR 0.61, 95% CI 0.38–0.96; P = 0.03). The incidence of grade 3-4 adverse events (AEs) was 11.2% in the Camrelizumab Arm and 3.2% in the Standard-therapy Arm, including grade 3-4 immunerelated AEs in 8 (3.9%) patients in the Camrelizumab Arm. Reactive capillary endothelial proliferation was the most common adverse event related to camrelizumab (RECP, 87.8%, 4 (1.8%) patients had grade 3 RECP). Treatment-related deaths occurred in 1 (,1%) patients in the Camrelizumab group (subarachnoid hemorrhage) and 1 (,1%) patients in the Standardtherapy group (nasopharyngeal necrosis). During treatment, there was no clinically meaningful deterioration of health-related quality of life associated with the use of adjuvant camrelizumab.

Conclusions: Adjuvant PD-1 blockade with camrelizumab significantly improved EFS in highrisk locoregionally advanced NPC, with mild toxicity and comparable quality of life. Clinical trial information: NCT03427827. Research Sponsor: Jiangsu Hengrui Pharmaceuticals.

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Phase III randomized trial of intensity-modulated proton therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for the treatment of head and neck oropharyngeal carcinoma (OPC).

Steven J. Frank, Paul Busse, David Ira Rosenthal, Mike Hernandez, David Michael Swanson, Adam S. Garden, Erich M. Sturgis, Renata Ferrarotto, Gary Brandon Gunn, Samir H Patel, NANCY Y. LEE, Alexander Lin, James W Snider, Mark William McDonald, Christina Henson, Gopal Krishna Bajaj, Noah Kalman, Upendra Parvathaneni, Sanford R. Katz, Robert Leonard Foote, MD Anderson Clinical Trial Consortium; The University of Texas MD Anderson Cancer Center, Houston, TX; Massachusetts General Hospital, Boston, MA; Baylor College of Medicine, Houston, TX; Mayo Hosp, Phoenix, AZ; Memorial Sloan Kettering Cancer Center, New York, NY; University of Pennsylvania, Philadelphia, PA; The South Florida Proton Therapy Institute, Delray Beach, FL; Emory University Winship Cancer Institute, Atlanta, GA; Stephenson Cancer Center, University of Oklahoma, Oklahoma City, OK; Inova Fairfax Hospital, Fairfax, VA; Miami Cancer Institute, Miami, FL; University of Washington, Seattle, WA; WillisKnighton Medical Center, Shreveport, LA; Mayo Clinic Department of Pediatric and Adolescent Medicine, Rochester, MN

Background: IMPT has unique biologic and physical properties compared with IMRT, limits radiation dose beyond the targeted tumor volumes, and is a novel de-intensification strategy for the management of head and neck tumors. This study was designed to compare the outcomes for patients with OPC after chemoradiation therapy (CRT) with IMRT vs IMPT.

Methods: This is a multi-center, randomized, phase III non-inferiority OPC trial Stage III/ IV (AJCC 7th) squamous cell carcinoma stratified patients by human papillomavirus status, smoking status, and receipt of induction chemotherapy (IC). The primary endpoint was the rate of progression-free survival (PFS) rate at 3 years, where progression was defined as disease recurrence or death. Under the null hypothesis, H0: r $ 1.535 established the margin for noninferiority of IMPT. Secondary endpoints include overall survival (OS), treatment-related malnutrition, and gastrostomy-tube dependence. Analyses were conducted on intent-totreat (ITT; n=440), per-protocol (PP; n=296), and as-treated (AT; n=397) populations.

Results: Patients (n=440) were randomized to undergo IMRT(n=219) or IMPT (n=221) at 21 institutions. The median age was 61 years and HPV/p16 was positive in 95%. IC was the initial treatment in 13% of patients. All patients were treated with CRT to 70 Gy in 33 fx with bilateral neck treatment, and post-CRT surgical lymph node dissection occurred in 8%. The median follow-up was 3.14 years. In the ITT analysis, the hazard ratio (HR) for disease progression or death at 3 y was 0.87 (95%CI 0.56,1.35); p=0.006 and the corresponding HR for death (OS) was 0.63 (95%CI 0.36-1.10) suggesting a protective affect with IMPT. In PP analysis, the PFS HR was 0.85 (95%CI 0.52,1.38); p=0.009 and HR for death (OS) was 0.60 (95%CI 0.32-1.12). In the AT analysis, PFS HR was 0.88 (95%CI 0.56,1.37); p=0.007 and the corresponding HR for death (OS) was 0.70 (95%CI 0.40-1.22). For each analysis above, the null hypothesis was rejected and IMPT was non-inferior to IMRT. PP gastrostomy-tube dependence decreased with IMPT vs. IMRT from 42% to 28% (p=0.019), and more IMPT patients sustained their nutrition with end of treatment weight loss , 5% from baseline: 24% vs 14% (p=0.037).

Conclusions: IMPT is noninferior to IMRT and has emerged as a standard of care CRT approach for OPC that reduces malnutrition and gastrostomy-tube dependence. Clinical trial information: NCT01893307. Research Sponsor: Hitachi.

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Nivolumab (NIVO) plus ipilimumab (IPI) vs lenvatinib (LEN) or sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC): First results from CheckMate 9DW.

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Background: First-line therapies based on programmed death ligand 1 (PD-L1) inhibitors are standard of care (SOC) in uHCC and demonstrate improved outcomes over SOR; however, prognosis remains poor and there is an unmet need for alternative therapies with long-term benefits. Second-line NIVO + IPI demonstrated clinically meaningful efficacy and manageable safety in SOR-treated patients (pts) with HCC in CheckMate 040, leading to its accelerated approval in the United States. We report first results from the preplanned interim analysis of the phase 3, open-label, randomized CheckMate 9DW trial evaluating the efficacy and safety of NIVO + IPI vs LEN or SOR as first-line therapy for pts with uHCC (NCT04039607). Methods: Adult pts with previously untreated HCC not eligible for curative surgical or locoregional therapies, Child-Pugh score 5–6, and ECOG performance status 0–1 were included. Pts were randomly assigned 1:1 to receive NIVO 1 mg/kg + IPI 3 mg/kg Q3W (up to 4 cycles) followed by NIVO 480 mg Q4W or investigator's choice of LEN 8 mg or 12 mg QD or SOR 400 mg BID until disease progression or unacceptable toxicity. NIVO was given for a maximum of 2 years. The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR) and duration of response (DOR) per blinded independent central review (BICR) using RECIST v1.1.

Results: In total, 668 pts were randomized to NIVO + IPI (n = 335) or LEN/SOR (n = 333); among 325 pts treated in the LEN/SOR arm, 275 (85%) received LEN. After a median (range) follow-up of 35.2 (26.8–48.9) months (mo), median OS was 23.7 mo with NIVO + IPI vs 20.6 mo with LEN/SOR (HR, 0.79; 95% CI, 0.65–0.96; P = 0.0180) (Table), with respective 24- mo OS rates (95% CI) of 49% (44–55) vs 39% (34–45). ORR was higher with NIVO + IPI (36%) vs LEN/SOR (13%; P , 0.0001); complete response was observed in 7% of pts with NIVO + IPI vs 2% with LEN/SOR. Median DOR was 30.4 mo with NIVO + IPI vs 12.9 mo with LEN/SOR (Table). A summary of treatment-related adverse events (TRAEs) is shown in the Table.

Conclusions: NIVO + IPI demonstrated statistically significant OS benefit vs LEN/SOR in pts with previously untreated uHCC, as well as higher ORR and durable responses with a manageable safety profile. These results support this combination as a potential new first-line SOC for uHCC. Clinical trial information: NCT04039607. Research Sponsor: Bristol Myers Squibb.

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Chemotherapy and liver transplantation versus chemotherapy alone in patients with definitively unresectable colorectal liver metastases: A prospective multicentric randomized trial (TRANSMET).

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Background: Despite the increasing efficacy of chemotherapy (CT) and advances in surgical techniques for initially unresectable colorectal liver metastases (uCLM), secondary resection rate remains low. For definitively uCLM, CT remains the standard of care but liver transplantation (LT) has shown promising results. This first randomized trial aimed to assess the efficacy of CT combined to LT for uCLM.

Methods: Patients with definitively uCLM from resected BRAF non mutated colorectal cancer, having responded to CT ($ 3 months and # 3 lines) in the absence of extrahepatic disease, were validated by an independent experts' committee and randomly assigned (1:1) to receive CT and LT (CT+LT arm) or CT alone (CT arm). The primary endpoint was 5-year overall survival (OS). Secondary endpoints were progression free survival (PFS) and patterns of recurrence. In order to detect a 40% difference in OS from 10% (CT) to 50% (CT+LT) (2-sided a level 5% - 90% power), 29 events were initially needed, secondly re-estimated to 50 according to the rate of patients not receiving LT in the CT+LT arm during the study.

Results: Between February 2016 and July 2021, 94 patients (median age 54 years, IQR 47-59) were randomly assigned to CT+LT arm (n = 47) or CT arm (n = 47). Median number and maximal diameter of uCLM at diagnosis were 20 (13-25) and 51.5 (37-78) mm, respectively. At randomization, objective response was obtained after a median number of 20 (14-27) CT cycles during 1 (44%), 2 (40%) or 3 (16%) lines. Median delay between primary tumour resection and randomisation was 14.6 (10.6-22.3) months. In CT+LT arm, 38 (81%) underwent LT after a median of 51 (30-65) days from randomization. Nine patients did not receive LT because of tumour progression during the waiting time or intraoperative finding of extrahepatic disease. Three (8%) of the 38 transplanted patients were retransplanted, one of whom (3%) died postoperatively. Post-transplant CT was administered in 26 (68%) patients. In CT arm, 9 (19%) patients unexpectedly underwent partial hepatectomy (7) or LT (2). In intent-to-treat analysis, 5-year OS was 57% in CT+LT arm and 13% in CT alone arm (log-rank test: p = 0.0003 - HR 0.37; 95%CI 0.21-0.65). In per protocol analysis, 5-year OS rate was 73% and 9%, respectively (HR 0.16; 95%CI 0.07-0.33). Median PFS was 17.4 months versus 6.4 months (HR 0.34; 95%CI 0.20-0.58), respectively. Among transplanted patients, 28 (74%) had lung (39%), liver (3%), other (21%) or multisite (11%) recurrence, optionally treated by surgery (36%) or local ablation (11%). Fifteen (40%) patients were ultimately disease-free.

Conclusions: LT combined with CT significantly improved survival in selected patients with uCLM compared to CT alone. These results argue for validating LT as a new standard option that may change the treatment strategy for liver-only uCLM patients. Clinical trial information: NCT02597348. Research Sponsor: Institut National du Cancer, Programme Hospitalier de Recherche Clinique du Cancer, Ligue Contre le Cancer.

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Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer: Overall survival and updated 5-year results from the randomized DYNAMIC trial.

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Background: Previous results of the DYNAMIC study demonstrated that a ctDNA-guided approach versus standard management in stage II colon cancer (CC) reduced adjuvant chemotherapy (ACT) use without compromising 2-year recurrence-free survival (RFS). MMR status defines two distinct subsets of stage II CC. Here, we report the impact of ctDNA burden, end of ACT (EOT) ctDNA, and updated survival data including overall survival (OS).

Methods: DYNAMIC is a multi-center randomized phase II trial. Eligible patients (pts) had resected stage II CC and were suitable for ACT. Pts were randomly assigned 2:1 to ctDNA-guided management or standard management (clinician-guided based on conventional criteria). For ctDNA-guided management, a ctDNA-positive result at 4 or 7 weeks after surgery with a tumor-informed assay prompted oxaliplatin-based or fluoropyrimidine ACT; ctDNA-negative pts were not treated. Between Aug 2015 and Aug 2019, 302 received ctDNA-guided and 153 standard management. The primary endpoint was RFS, with a non-inferiority margin of 8.5%. Prespecified key secondary endpoints were ACT use and OS, with an additional secondary endpoint of ctDNA clearance rate.

Results: With a median follow-up of 59.6 months (IQR 55.0–61.5), 5- year RFS were 88% and 87% with ctDNA-guided and standard management, respectively (difference 1.1%, 95% confidence interval, -5.8% to 8.0%). 5-year OS for ctDNA-guided treatment was 93.8% and standard management 93.3% (HR 1.05; 95% CI, 0.47 to 2.37; P = 0.887). 5-year OS was significantly worse in treated ctDNA-positive versus untreated ctDNAnegative pts (85.6% vs 95.3%, HR 3.30; 95% CI, 1.02 to 9.05; P = 0.014). The 5-year OS for ctDNA-negative T3 and T4 disease were 96.0% and 90.6%, respectively (HR 2.45; 95% CI, 0.65 to 9.25; P = 0.171). For treated ctDNA-positive pts, ctDNA clearance was observed at EOT in 35/ 40 (87.5%). The 5-year RFS for EOT ctDNA clearance vs ctDNA persistence were 85.2% and 20.0%, respectively (HR 15.4; 95% CI, 3.91 to 61.0; P , 0.001). Pts with $ 0.38 (the median) mutant tumor molecules (MTM/mL) had a lower ctDNA clearance rate and worse RFS than pts with , 0.38 MTM/mL (ctDNA clearance 75% vs 100%, P = 0.047; 5-year RFS 58.9% vs 95.2%, HR 10.62, P = 0.005). Post-op ctDNA was detected in 5/59 (8.5%) of dMMR and 40/235 (17%) of pMMR cases. In an exploratory analysis, ctDNA clearance was observed in 3/4 (75%) and 32/36 (89%) of dMMR and pMMR cases, respectively.

Conclusions: Mature outcome data confirms the previous finding of non-inferiority of RFS with a ctDNA-guided approach to ACT for stage II CC. For ctDNA-positive pts, the post-surgery mutation burden provides additional prognostic information, as does the EOT ctDNA result. Additional data is needed to define any differential impact of ACT by MMR status. This data supports a role for ctDNA analysis, including serial sampling, in the management of stage II CC. Clinical trial information: ACTRN12615000381583. Research Sponsor: NHMRC; U.S. National Institutes of Health.

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Nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) as first-line (1L) treatment for microsatellite instability-high/mismatch repair-deficient (MSI-H/ dMMR) metastatic colorectal cancer (mCRC): Expanded efficacy analysis from CheckMate 8HW.

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Background: NIVO + IPI demonstrated superior progression-free survival (PFS) vs chemo in patients (pts) with previously untreated MSI-H/dMMR mCRC in the randomized phase 3 CheckMate 8HW study (NCT04008030). We report expanded efficacy analysis from the prespecified interim analysis of NIVO + IPI vs chemo in the 1L setting.

Methods: Pts with unresectable or mCRC and MSI-H/dMMR status by local testing were enrolled across different lines of therapy and randomized 2:2:1 to NIVO (240 mg) + IPI (1 mg/kg) Q3W (4 doses, then NIVO 480 mg Q4W), NIVO (240 mg) Q2W (6 doses, then NIVO 480 mg Q4W), or chemo 6 targeted therapies; treatments continued until disease progression or unacceptable toxicity (all arms) or for up to 2 years (NIVO 6 IPI arms). In pts with blinded independent central review (BICR)– documented progression with chemo, crossover to NIVO + IPI was permitted. Dual primary endpoints were PFS by BICR per RECIST v1.1 for NIVO + IPI vs chemo (1L) and NIVO + IPI vs NIVO (all lines) in pts with centrally confirmed MSI-H/dMMR mCRC. PFS2 (time from randomization to progression after subsequent systemic therapy, initiation of second subsequent systemic therapy, or death) was a key exploratory endpoint.

Results: Among 303 pts randomized to NIVO + IPI (n = 202) or chemo (n = 101), 171 pts in the NIVO + IPI arm and 84 pts in the chemo arm had centrally confirmed MSI-H/dMMR. At 31.5-months (mo) median follow-up (range 6.1–48.4), NIVO + IPI demonstrated superior PFS vs chemo (HR 0.21; 97.91% CI 0.13–0.35; P , 0.0001). Subsequent systemic therapy was received by 20 (12%) and 57 (68%) pts in the NIVO + IPI and chemo arms, respectively. In the chemo arm, 56 (67%) pts received subsequent immunotherapy (39 [46%] crossed over to NIVO + IPI on study; 17 [20%] received non-study immunotherapy). Median PFS2 was not reached (NR) with NIVO + IPI and 29.9 mo with chemo (HR 0.27; 95% CI 0.17–0.44; Table). Any grade and grade 3/4 treatment-related adverse events (TRAEs) are presented (Table). Treatment-related deaths were reported for 2 pts in the NIVO + IPI arm.

Conclusions: Clinical benefit with 1L NIVO + IPI vs chemo was maintained after subsequent therapy, as shown by improved PFS2 in pts with centrally confirmed MSI-H/dMMR mCRC. No new safety concerns were identified with NIVO + IPI. These results further support NIVO + IPI as a standard-of-care 1L treatment option for pts with MSI-H/ dMMR mCRC. Clinical trial information: NCT04008030. Research Sponsor: Bristol Myers Squibb.

LBA3501

Surgery versus thermal ablation for small-size colorectal liver metastases (COLLISION): An international, multicenter, phase III randomized controlled trial.

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Background: The standard of care for local treatment of patients (pts) with colorectal liver metastases (CRLM) is surgical resection. However, growing evidence suggests thermal ablation to be associated with a superior safety profile, lower costs, and shorter hospital stay, while rivaling surgical resection in terms of local control and overall survival (OS). This study aimed to explore the potential non-inferiority of thermal ablation compared to surgical resection for pts with small-size (#3cm) resectable CRLM.

Methods: In this multicenter, phase 3 Dutch Colorectal Cancer Group trial, pts aged 18 years and older with previously untreated CRLM were recruited from 14 centers in the Netherlands, Belgium and Italy. Pts with #10 CRLM, no extrahepatic metastases and ECOG 0-2 were stratified into low, intermediate and high disease burden subgroups and randomly assigned (1:1) to undergo surgical resection or thermal ablation. Though approach was left at the discretion of the operator, laparoscopic (+/- robot) resections and percutaneous ablations were favored over open procedures. To avoid drop-outs patients undergoing open procedures were randomized intra-operatively. The primary outcome was overall survival (OS) (log-rank; power 80%, 5% type I error rate; 1-sided). Secondary outcomes include distant and local tumor progression-free survival (PFS), local control, safety, length of hospital stay, quality of life and cost-effectiveness.

Results: A total of 341 patients were enrolled; 299 were randomly assigned: 147 assigned to thermal ablation, 148 to surgical resection; 4 were excluded after randomization for not having the disease assessed. The trial was stopped at halftime for having met predefined stopping rules. After a median follow-up time of 28.8 months there was no difference regarding OS (HR 1.042; 95% CI, 0.689-1.576; p = 0.846) with a conditional probability of .90% to prove the hypothesis of non-inferiority. Procedure related mortality was 2.1% (n=3) for resection vs. 0% (n=0) for thermal ablation. The total number of adverse events (p = ,0.001), the length of hospital stay (median 4 days [range 1- 36] vs 1 day [range 1-44], p = ,0.001) and local control also favored thermal ablation (HR 0.184; 95% CI, 0.040-0.838; p = 0.029). No differences were found regarding local (HR 0.833; 95% CI, 0.473-1.469; p = 0.528) and distant PFS (HR 0.982; 95% CI, 0.739-1.303; p = 0898).

Conclusions: In conclusion, transitioning from surgical resection to thermal ablation as standard of care for patients with small-size (#3 cm) CRLM would reduce complications, shorten hospital stay and improve local control, without compromising disease-free and overall survival. COLLISION is funded by a Medtronic-Covidien Investigator Sponsored Research grant. Clinical trial information: NCT03088150. Research Sponsor: Medtronic Covidien; 20130529

LBA2

Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial.

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Background: Standard of care (SOC) for resectable, macroscopic stage III melanoma is therapeutic lymph node dissection (TLND) followed by adjuvant (adj) therapy with nivolumab (NIVO), pembrolizumab (PEM) or, in BRAFmut melanoma, dabrafenib + trametinib (DAB/ TRAM). The recent phase 2 SWOG S1801 trial showed superior event-free survival (EFS) of neoadjuvant (neoadj) + adj PEM as compared to adj PEM (estimated 2y-EFS 72% vs 49%). Additional phase 2 trials demonstrated safety and high efficacy (77-80% 2y-EFS) of neoadj ipilimumab (IPI) 1 mg/kg + nivolumab (NIVO) 3 mg/kg, providing the rationale for testing neoadj IPI + NIVO against SOC in a phase 3 trial.

Methods: In this investigator initiated, international phase 3 trial, resectable, macroscopic, nodal stage III melanoma pts , naive to ICI and BRAFi/MEKi, were randomized to receive 2 cycles of neoadj IPI 80mg + NIVO 240mg (q3w) followed by TLND, and in case of not achieving a major pathologic response (MPR) adj DAB/TRAM (150mg BID/2mg QD; 46 wks) or 11 cycles of adj NIVO (480mg; q4w; if BRAFwt) versus TLND followed by 12 cycles of adj NIVO (480mg; q4w). The primary endpoint EFS is defined as time from randomization until progression, recurrence or death due to melanoma or treatment, and was assessed using a Cox regression model. An interim analysis using a 2-sided alpha of 0.1% (Haybittle-Peto stopping rule) was planned per protocol after completing recruitment.

Results: Between Aug 2021 and Dec 2023, 423 pts were randomly assigned; 212 pts to the neoadj arm and 211 to the adj arm. At data cutoff on January 12, 2024, with a median FU of 9.9 mos, significantly less events occurred in the neoadj arm vs the adj arm (28 vs 72), with HR 0.32 (99.9% CI 0.15-0.66, p,0.0001) and estimated 12-mo EFS rates of 83.7% (99.9% CI 73.8-94.8) vs 57.2% (99.9% CI 45.1-72.6) favoring the neoadj arm. In the subgroup of BRAFmut melanoma, estimated EFS rates were 83.5% and 52.1%, and in BRAFwt 83.9% and 62.4% for neoadj versus adj respectively. 58.0% of pts in the neoadj arm had an MPR, 8.0% a path partialresponse (pPR), 26.4% a path non-response (pNR), 2.4% had progression before surgery and 5.2% were not reported (95% centrally reviewed). The 12-mo RFS rates according to path response were 95.1% for MPR, 76.1% for pPR and 57.0% for pNR. Systemic treatment related adverse events (AE) grade $3 were seen in 29.7% and 14.7% in the neoadj and adj arm; 1 pt died due to toxicity in adj arm (pneumonitis). Surgery related grade $3 AEs were reported in 14.6% and 14.4% respectively.

Conclusions: NADINA is the first phase 3 trial that evaluates neoadj immunotherapy against SOC in melanoma, and is also the first phase 3 trial in oncology evaluating a neoadj regimen consisting of immunotherapy alone. Neoadj IPI+NIVO followed by response-driven adj treatment results in statistically significant improved EFS compared to adj NIVO and should be considered a new SOC treatment in macroscopic stage III melanoma. Clinical trial information: NCT04949113. Research Sponsor: Bristol Myers-Squibb; Australian Government.

LBA3

Comparative effectiveness trial of early palliative care delivered via telehealth versus in person among patients with advanced lung cancer.

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Background: National guidelines recommend the early integration of palliative and oncology care for patients with advanced cancer, given robust evidence showing that this care model improves quality of life (QOL) and other important outcomes. However, most patients do not receive early palliative care (EPC) in the outpatient setting due to limited access and resources. To overcome these barriers, we conducted a large-scale comparative effectiveness trial of EPC delivered via secure video versus in person among patients with advanced non-small cell lung cancer (NSCLC) and their caregivers.

Methods: Between 6/14/2018 and 5/4/2023, we enrolled 1250 patients with advanced NSCLC, diagnosed in the past 12 weeks, into a randomized trial of telehealth versus in-person EPC across 22 cancer centers in the US. Patients were randomly assigned to meet with a palliative care clinician every four weeks from enrollment through the course of disease either via video or in the outpatient clinic. Participants completed self-report measures at baseline and weeks 12 and 24. The primary aim was to evaluate the equivalence of the effect of telehealth versus in-person EPC on QOL at week 24, using regression modeling with an equivalence margin of 64 points on the Functional Assessment of Cancer TherapyLung (FACT-L, range = 0-136). We also compared rates of caregiver participation in EPC visits and patient-reported depression and anxiety symptoms (Patient Health Questionnaire-9; Hospital Anxiety and Depression Scale), coping (Brief COPE), and perceptions of prognosis (Perceptions of Treatment and Prognosis Questionnaire) between groups. Study recruitment ceased for two months at the onset of the COVID-19 pandemic.

Results: Participants (mean age = 65.5 years; 54.0% female; 82.1% White) had a mean of 4.75 and 4.92 palliative care encounters by week 24 in the telehealth and in-person groups, respectively. Due to the pandemic, the inperson group had 3.9% of visits occur via video. QOL scores at week 24 for patients assigned to the telehealth group were equivalent to those receiving in-person EPC (adjusted means: 99.67 versus 97.67, p , 0.043 for equivalence). The rate of caregiver participation in EPC visits was lower in the telehealth versus in-person group (36.6% versus 49.7%, p , 0.0001). Study groups did not differ in depression and anxiety symptoms, use of coping skills, or perceptions of the goal of treatment and curability of their cancer.

Conclusions: The delivery of EPC via video versus in-person visits demonstrated equivalent effects on QOL in patients with advanced NSCLC. The two modalities also did not differ across a range of patient-reported outcomes, though caregivers attended more in-person versus video visits. The findings underscore the considerable potential for improving access to and broader dissemination of this evidencebased care model through telehealth delivery. Clinical trial information: NCT03375489. Research Sponsor: Patient Centered Outcomes Research Institute; PLC-1609-35995

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A randomized, double-blind controlled trial of medicinal cannabis vs placebo for symptom management in patients with advanced cancer receiving palliative care.

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Background: Medicinal cannabis remains very popular amongst cancer patients. In our previous study (JCO 2023; 41(7):1444-1452), cannabidiol (CBD) did not improve symptom management above that provided by standard palliative care alone. This studytilized the same design to test whether the addition of tetrahydrocannabinol (THC) to CBD resulted in improved symptom control.

Methods: Patients with advanced cancer and a total symptom distress score (TSDS) of $10/90 as measured by the Edmonton Symptom Assessment Scale (ESAS) who were receiving palliative care were randomised to a 10mg/ml THC: 10mg/ml CBD combination oil (MC) or matched placebo. The dose was escalated according to tolerance and perceived efficacy from 2.5 to 30mg/day over 14 days and continued at that dose to day 28. The primary outcome was the change in TSDS from baseline at day 14. Secondary outcomes included change in individual symptoms, patient-selected dose, global impression of change, anxiety/depression, opioid use, quality of life and toxicity.

Results: Of the 144 randomized from Sept 2019 to July 2023 (72 to MC, 72 to placebo), 56 and 65 participants reached the primary analysis point at 14 days, and 33 and 50 to day 28. The most common cancers were breast, lung and gynecological. Most participants were of reasonable performance status (AKPS 70%) and were taking opioids at baseline. Mean baseline TSDS scores were 37.6/90 (MC) and 36.5/90 (placebo). Mean TSDS scores fell over time with no difference between arms at day 14 (-6.3 (SD 12.3) MC and -6.98 (SD 12.6), p = 0.76) or day 28 (-9.24 (SD 15.3) and 8.42 (SD 13.6), p = 0.8). Adjusted for baseline, there was a significant improvement in pain score from baseline in favor of MC (-1.41 (2.15) vs -0.46 (2.82), p = 0.04) and in overall wellbeing in favor of placebo (-0.48 (2.78) and -1.29 (2.74), p = 0.02) at day 14. The median (range) patient selected dose of oil at day 14 was 1.5ml (0.5-3.0) (equivalent to a dose of 15mgTHC/15mg CBD) and 3.0ml (0.5-3.0) for placebo. Side-effects were generally mild. More participants on MC reported confusion (26/69 and 12/72, p = 0.005), feeling high (21/69 and 10/72, p = 0.02) and an exaggerated sense of well-being (10/69 and 2/72, p = 0.01) as worse than baseline. Those on MC reported an improved global impression of change over time but this lost significance when considering those who exited early.

Conclusions: Although showing no advantage over placebo with respect to improving total symptom distress, a 1:1 THC:CBD medicinal cannabis oil resulted in a statistically significant improvement in cancer-related pain at the expense of increased psychomimetic toxicity. Trial registration: ACTRN 12619000037101. Sponsor: Australian Government Medical Research Future Fund. Clinical trial information: ACTRN12619000037101. Research Sponsor: Medical Research Future Fund; APP1152232.

4509

Characterization of complete responders to nivolumab + gemcitabine-cisplatin vs gemcitabine-cisplatin alone and patients with lymph node–only metastatic urothelial carcinoma from the CheckMate 901 trial.

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Background: In the CheckMate 901 trial, combination nivolumab (NIVO) + gemcitabine/cisplatin (GC) demonstrated significant improvements in overall survival (OS) and progression-free survival (PFS) with compelling objective response rates (ORR; 57.6% with NIVO+GC vs 43.1% with GC alone) and deep, durable complete responses (CR; 21.7% with NIVO+GC vs 11.8% with GC alone) in patients (pts) with previously untreated unresectable or metastatic urothelial carcinoma (mUC). Lymph node (LN)-only metastatic disease is a favorable prognostic factor in pts with mUC and a subset of pts achieve durable disease-free, treatment-free survival with GC +/- surgical consolidation. We conducted a post hoc analysis to characterize the subset of pts with CR, with further analysis of pts with LN-only mUC.

Methods: In the global, open-label, randomized, phase 3 CheckMate 901 (NCT03036098) trial, cisplatin-eligible pts received NIVO 360 mg + GC every 3 wk for #6 cycles followed by NIVO 480 mg every 4 wk until disease progression/ unacceptable toxicity or up to a maximum of 2 yrs, or GC every 3 wk for #6 cycles. Primary endpoints were OS and PFS by blinded independent central review (BICR). ORR per BICR and safety were exploratory endpoints. These post hoc analyses evaluated treatment outcomes in complete responders and in pts with LN-only disease.

Results: Of the 608 pts randomized, 102 (16.8%) achieved a CR. Baseline disease characteristics of these pts are shown in the Table. As pts with LN-only mUC were enriched in the CR group, additional analysis of this subgroup was performed. Of all randomized pts, 54 treated with NIVO+GC and 56 treated with GC had LN-only mUC. In these pts, the ORR and CR rate was 81.5% (95% CI 68.6-90.7) and 63.0% versus 64.3% (50.4-76.6%) and 33.9% for NIVO+GC and GC, respectively. Median OS (95% CI) in LN-only pts was 46.3 (24.0-NE) mos with NIVO+GC vs 24.9 (21.4-29.9) with GC (HR, 0.58, 95% CI 0.34-1.00), and median PFS (95% CI) was 30.5 (9.6-NE) mos with NIVO+GC vs 8.8 (7.5-10.9) mos with GC (HR 0.38, 95% CI 0.22- 0.66).

Conclusions: NIVO+GC generated deep responses in CheckMate 901 with a fixed duration of chemotherapy and up to 2 years NIVO. Exploratory characterization of pts with CR identified a group of pts enriched with LN-only disease. In pts with LN-only mUC, NIVO+GC induced durable disease control and clinically meaningful improvements in OS and PFS vs GC alone. These results provide additional support for NIVO plus cisplatin-based chemo as a firstline treatment option for pts with mUC. Clinical trial information: NCT03036098. Research Sponsor: Bristol Myers Squibb.

10500

Effect of polygenic risk score for clinically significant prostate cancer in a screening program: The BARCODE 1 study results.

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Background: Incidence of prostate cancer (PCa) is increasing, but there is no internationally agreed population screening program. Studies using an age-based PSA approach show a high rate of false-positive results as well as over-diagnosis of indolent PCa. Genome wide association studies identify common germline variants to calculate a polygenic risk score (PRS) associated with PCa risk. The BARCODE1 study used PRS to target PCa screening to those at higher risk based on genotype.

Methods: European men aged 55-69yrs were recruited via Primary Care in the UK. PRS was constructed by summing weighted risk alleles for 130 PCa risk variants using germline DNA from saliva samples via mailed kits. Men with a PRS . 90th centile were invited for PCa screening using MRI and 12-core transperineal biopsy (including MRI fusion to target additional lesions where identified) irrespective of PSA result.

Results: Invitation letters were sent to 40,292 men. 8,953 (22%) expressed an interest; 8,014 were eligible and sent a saliva kit. 6,644 consented; 6,393 were genotyped; 251 failed QC. A total of 6,142 participants had PRS calculated: 745 (12.1%) had a PRS . 90th centile and were invited to screening. 558/745 participants attended screening (121 declined, 66 excluded on health grounds). 551 underwent MRI and 468 had prostate biopsy resulting in 187 (40.0%) diagnoses of PCa, overall PCa detection rate 2.8%. Mean age at diagnosis 64.1yrs (range 57-73; median 64). Using NCCN criteria (2023) 103/187 (55.1%) of cancers were Intermediate or High Risk; 40/187 (21.4%) were Intermediate Unfavourable/ High/Very High Risk. 119/187 (63.6%) men had a PSA ,3.0ug/L; PPV of biopsy for PSA . 3.0ug/L was 49.6%. PPV of MRI (presence of PI-RADS 3- 5 lesion) 60.4%. PPV of PRS alone 40%. 103/187 (55.1%) had Gleason .7; compared with 360/ 1014 (35.5%) p , 0.001 in the PSA directed ERSPC study.

Conclusions: A population PCa screening program using PRS risk-stratification enriches for clinically significant PCa requiring treatment. It detects a high proportion of clinically significant disease compared with PSA or MRI based screening programs and MRI missed a significant proportion (17-67%) of cancers found on biopsy. This is the first study to assess if this approach will be useful in population screening programs. Clinical trial information: NCT03857477. Research Sponsor: The European Research Council; ERC-2013-AdG-339208; Cancer Research UK; EDDCPJT\ 100006; National Institute for Health Research (NIHR) to the Biomedical Research Centre at The Institute of Cancer Research and Royal Marsden Foundation NHS Trust; The Bob Willis Fund.

LBA4

Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study.

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Background: EGFR mutations occur in up to one-third of pts with unresectable stg III NSCLC. Consolidation durvalumab is standard of care (SoC) for pts who do not progress after concurrent CRT (cCRT), yet the benefit of consolidation immunotherapy specifically for EGFRm NSCLC remains uncertain, with limited data available. Osi, a 3rd-generation CNS-active EGFR-TKI, is recommended for EGFRm advanced/metastatic NSCLC and as adjuvant therapy for resectable EGFRm NSCLC. We report primary results from the global, double-blind, placebo (PBO)-controlled Phase 3 LAURA study (NCT03521154), assessing efficacy/safety of osi in unresectable stg III EGFRm NSCLC without progression after definitive CRT.

Methods: Eligible pts: aged $18 years ($20 in Japan), WHO PS 0/1, unresectable stg III EGFRm (Ex19del/L858R) NSCLC, had received definitive platinum-based cCRT/sequential CRT (sCRT) with no progression. Pts were stratified (cCRT vs sCRT; stg IIIA vs IIIB/IIIC; Chinese vs non-Chinese) and randomized 2:1 to receive osi 80 mg or PBO QD until progression (blinded independent central review [BICR]- confirmed)/discontinuation. Imaging, including brain MRI, was mandated at baseline, every 8 wks to wk 48, then every 12 wks, until progression by BICR. Open-label osi was offered after progression by BICR. Primary endpoint: progression-free survival (PFS; RECIST v1.1) assessed by BICR. Secondary endpoints included overall survival (OS) and safety. Data cut-off: January 5, 2024.

Results: Overall, 216 pts were randomly assigned: osi n=143, PBO n=73. Baseline characteristics were generally balanced across osi/PBO arms: female 63/58%, stg IIIA 36/33%, IIIB 47/52%, IIIC 17/15%, Ex19del 52/59%. Osi significantly improved PFS by BICR vs PBO: HR 0.16; 95% CI 0.10, 0.24; p,0.001. Median PFS was 39.1 mo (95% CI 31.5, not calculable) for osi vs 5.6 mo (95% CI 3.7, 7.4) for PBO; 12-mo PFS rate was 74% (osi) vs 22% (PBO); 24-mo PFS rate was 65% (osi) vs 13% (PBO). Investigator-assessed PFS (HR 0.19; 95% CI 0.12, 0.29; nominal p,0.001) was consistent with PFS by BICR. PFS benefit was consistent across predefined subgroups. Interim OS analysis (20% maturity) showed a trend in favor of osi: HR 0.81; 95% CI 0.42, 1.56; p=0.530; 81% of pts (PBO arm) received osi after

progression. Allcausality AEs were reported in 98% vs 88% pts; $Grade 3 AEs in 35% vs 12%; serious AEs in 38% vs 15% for osi vs PBO, respectively. Radiation pneumonitis AEs (grouped term): 48% (osi) vs 38% (PBO), majority Grade 1/2. Any AEs leading to discontinuation were reported in 13% vs 5% for osi vs PBO, respectively.

Conclusions: Osi after definitive CRT demonstrated a statistically significant and clinically meaningful improvement in PFS, for unresectable stg III EGFRm NSCLC, with no unexpected safety signals. These results establish osi as the new SoC for EGFRm NSCLC in this setting. Clinical trial information: NCT03521154. Research Sponsor: AstraZeneca.

LBA8505

Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory EGFR-mutated, advanced non-small cell lung cancer (NSCLC): Primary results, including overall survival (OS), from the global, phase 3, randomized controlled PALOMA-3 trial.

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Background: Amivantamab (ami) plus lazertinib (laz) demonstrated antitumor activity in EGFR-mutated advanced NSCLC. Subcutaneous (SC) ami administration takes #7 mins and has low infusion-related reaction (IRR) rates. PALOMA-3 (NCT05388669) evaluated SC ami+- laz vs IV ami+laz for pharmacokinetics (PK), efficacy, and safety among pts with EGFR Ex19del or L858R-mutated advanced NSCLC and disease progression on osimertinib and platinumbased chemotherapy.

Methods: SC ami at 1600 mg (2240 mg, $80 kg) was manually injected weekly for the first 4 weeks, then every 2 weeks; IV ami was given at the approved dose of 1050 mg (1400 mg, $80 kg). Laz was orally dosed at 240 mg daily. Co-primary PK noninferiority endpoints were trough concentration (Ctrough on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15). Key secondary endpoints were objective response rate (ORR; noninferior) and progression-free survival (PFS). OS was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first 4 months (mo) of treatment.

Results: In total, 418 patients (pts) were randomized (SC, n = 206; IV, n = 212); 416 received $1 dose. Overall, median age was 61 years, 67% were female, 61% Asian, and median 2 prior lines. At a median follow-up of 7.0 mo, PALOMA-3 met both co-primary endpoints. Geometric mean ratios (GMRs) comparing SC ami+laz vs IV for Ctrough were 1.15 (90% CI, 1.04–1.26) for C2D1 and 1.43 (90% CI, 1.27–1.61) for C4D1. GMR for C2 AUCD1-D15 was 1.03 (90% CI, 0.98–1.09). ORR was 30.1% (95% CI, 24–37) in the SC arm and 32.5% (95% CI, 26–39) for IV (relative risk, 0.92; P= 0.001), meeting the noninferiority criteria. Median duration of response (DoR) was longer for SC ami+laz vs IV (median, 11.2 vs 8.3 mo among confirmed responders). A favorable PFS trend was observed for SC ami+laz over IV (median, 6.1 vs 4.3 mo; HR, 0.84; P= 0.20). OS was notably longer for SC ami+laz vs IV (HR, 0.62; 95% CI, 0.42–0.92; nominal P= 0.017). At 12 mo, 65% were alive in the SC arm vs 51% for IV. IRRs were ~5-fold lower in the SC arm: 13% vs 66% for IV, primarily grade 1-2 (0.5% vs 4% grade $3, respectively). Overall, 81% received prophylactic anticoagulants, with VTE reported by 9% in the SC arm vs 14% for IV. Across both arms, VTE incidence was 10% for pts who received prophylactic anticoagulants vs 21% for pts who did not. Severe bleeding risk was low among all pts receiving anticoagulants (1% grade $3).

Conclusions: SC ami demonstrated noninferior PK and ORR compared to IV. Unexpectedly, DoR, PFS, and OS were longer in the SC arm vs IV, suggesting that the route of administration or formulation may affect outcomes. The safety profile was improved for SC ami, with lower IRR and VTE rates. Prophylactic anticoagulation can be safely implemented and reduces VTE risk. Clinical trial information: NCT05388669. Research Sponsor: Janssen Global Services LLC.

LBA5

ADRIATIC: Durvalumab (D) as consolidation treatment (tx) for patients (pts) with limited-stage small-cell lung cancer (LS-SCLC).

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Background: The standard of care (SoC) for pts with LS-SCLC is concurrent platinum-based chemoradiotherapy (cCRT) 6 prophylactic cranial irradiations (PCI). ADRIATIC (NCT03703297), a phase 3, randomized, double-blind, placebo (PBO)-controlled, multicenter, global study, assessed D 6 tremelimumab (T) as consolidation tx for pts with LS-SCLC who had not progressed after cCRT. Here we report results for D vs PBO from the first planned interim analysis (IA).

Methods: Eligible pts had stage I–III LS-SCLC (stage I/II inoperable) and WHO performance status 0/1, and had not progressed after cCRT. PCI was permitted before randomization. Pts were randomized 1–42 days after cCRT to D 1500 mg + PBO, D 1500 mg + T 75 mg, or PBO + PBO every 4 weeks (Q4W) for 4 cycles, followed by D (D6T arms) or PBO Q4W until investigator-determined progression or intolerable toxicity, or for a maximum of 24 months (mo). The first 600 pts were randomized in a 1:1:1 ratio; subsequent pts were randomly assigned 1:1 to D or PBO. Randomization was stratified by stage (I/II vs III) and receipt of PCI (yes vs no). The dual primary endpoints were OS and PFS (blinded independent central review per RECIST v1.1) for D vs PBO. OS and PFS for D+T vs PBO were alpha-controlled secondary endpoints.

Results: 730 pts were randomized, including 264 to D and 266 to PBO. Baseline characteristics and prior tx were well balanced between arms. Radiation schedule in the D vs PBO arms was once daily in 73.9% vs 70.3% of pts and twice daily in 26.1% vs 29.7%; 53.8% of pts in each arm received PCI. At this IA (data cutoff 15Jan2024), median (range) duration of follow-up for OS and PFS in censored pts was 37.2 (0.1–60.9) and 27.6 (0.0–55.8) mo, respectively. OS was significantly improved with D vs PBO (HR 0.73 [95% CI 0.57–0.93]; p=0.0104; median OS 55.9 [95% CI 37.3 – not estimable] vs 33.4 [25.5–39.9] mo; 24-mo OS rate 68.0% vs 58.5%; 36-mo OS rate 56.5% vs 47.6%). PFS was also significantly improved with D vs PBO (HR 0.76 [95% CI 0.61–0.95]; p=0.0161; median PFS 16.6 [95% CI 10.2–28.2] vs 9.2 [7.4–12.9] mo; 18-mo PFS rate 48.8% vs 36.1%; 24-mo PFS rate 46.2% vs 34.2%). Tx benefit was generally consistent across predefined pt subgroups for both OS and PFS. With D vs PBO, maximum grade 3/4 all-cause adverse events (AEs) occurred in 24.3% vs 24.2% of pts; AEs led to tx discontinuation in 16.3% vs 10.6% of pts and to death in 2.7% vs 1.9%. Any-grade pneumonitis/radiation pneumonitis was reported in 38.0% vs 30.2% of pts with D vs PBO (maximum grade 3/4 in 3.0% vs 2.6%). The D+T arm remains blinded until the next planned analysis.

Conclusions: D as consolidation tx after cCRT demonstrated a statistically significant and clinically meaningful improvement in OS and PFS compared with PBO in pts with LS-SCLC. D was well tolerated and AEs were consistent with the known safety profile, with no new signals observed. These data support consolidation D as a new SoC for pts with LS-SCLC who have not progressed after cCRT. Clinical trial information: NCT03703297. Research Sponsor: AstraZeneca.

8015

DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastasis.

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Background: Brain metastases affect 40%–70% of patients with SCLC. Tarlatamab, a BiTE (bispecific T-cell engager) immunotherapy targeting delta-like ligand 3, demonstrated durable responses and promising survival outcomes in patients with previously treated SCLC (10 mg Q2W) (DeLLphi-301; NCT05060016; Ahn M-J, N Engl J Med 2023). Here, tarlatamab efficacy and safety in patients with baseline brain metastases from DeLLphi-301 are reported. Methods: The DeLLphi-301 study design has been published. Patients with treated, stable, asymptomatic brain metastases were included. Subgroup analyses for efficacy (blinded independent central review [BICR] assessments) and safety by presence or absence of baseline brain metastases were performed. Intracranial activity was assessed. Post enrollment, brain imaging was performed if clinically indicated.

Results: As of 27 June 2023, 186 patients had received tarlatamab (ECOG PS: 0–1; median prior lines of therapy: 2; median follow-up: 13.6 months). 29% of patients (54/186) had treated and stable brain metastases at baseline. Most patients (91%) with brain metastases had received prior local radiotherapy; 6% each had received surgery only or both radiotherapy and surgery. Overall systemic objective response rate (ORR; RECIST 1.1) was 45.3% in patients with brain metastases and 32.6% in patients without brain metastases (Table). Any grade immune effector cell associated neurotoxicity syndrome and associated neurological events occurred in 24.1% of patients with brain metastases and in 13.6% of patients without brain metastases; grade $ 3 events occurred in the 100 mg group only: 9.4% and 1.8%, respectively, and did not lead to tarlatamab discontinuation in any patient with brain metastases. Analysis of intracranial activity will be presented.

Conclusions: Tarlatamab showed promising efficacy and a favorable benefit-risk profile in patients with previously treated SCLC and stable brain metastases. Clinical trial information: NCT05060016. Research Sponsor: Amgen Inc.

LBA8509

KRYSTAL-12: Phase 3 study of adagrasib versus docetaxel in patients with previously treated advanced/ metastatic non-small cell lung cancer (NSCLC) harboring a KRASG12C mutation.

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Background: Adagrasib (ADA) is a potent covalent inhibitor of KRASG12C with favorable properties such as long half-life (23 h), dose-dependent pharmacokinetics, and brain penetrance. In the phase 1/2 KRYSTAL-1 trial, ADA demonstrated deep and durable responses with promising PFS and OS in patients (pts) with previously treated KRASG 12C-mutated NSCLC. Here, we report the primary analysis from KRYSTAL-12 (NCT04685135), a randomized, open-label phase 3 trial of ADA compared with docetaxel (DOCE) in pts with KRASG12C-mutated locally advanced or metastatic NSCLC who had previously received a platinum-based chemotherapy, concurrently or sequentially with anti-PD-(L)1 therapy.

Methods: Pts with KRASG12C-mutated locally advanced or metastatic NSCLC, previously treated with platinum-based chemotherapy and antiPD-(L)1 therapy, were randomized 2:1 (stratified by region [non-Asia Pacific vs Asia Pacific] and sequential vs concurrent chemoimmunotherapy) to receive ADA (600 mg BID orally; tablet formulation) or DOCE (75 mg /m2 Q3W IV), with the ability to crossover to ADA upon disease progression (assessed by real-time blinded independent central review [BICR]). No washout period was required between prior anti-PD-(L)1 therapy and study treatment. Primary endpoint was PFS assessed per BICR according to RECIST v1.1. Secondary endpoints included ORR by BICR, duration of response (DOR), OS, 1-year OS rate, and safety.

Results: In total, 301 pts were randomized to ADA and 152 to DOCE. Baseline characteristics were generally similar between treatment arms. With a median follow-up of 9.4 mo (data cutoff 31 Dec, 2023), the primary endpoint of PFS was significantly improved with ADA over DOCE (HR 0.58 [95% CI, 0.45–0.76]; P , 0.0001; median PFS 5.49 vs 3.84 mo). ORR by BICR was also significantly higher with ADA compared with DOCE (31.9% [95% CI, 26.7–37.5] vs 9.2% [95% CI, 5.1–15.0]; odds ratio 4.68 [95% CI, 2.56–8.56]; P , 0.0001); median DOR was 8.31 (95% CI, 6.05–10.35) vs 5.36 (95% CI, 2.86–8.54) mo, respectively. Treatment-related adverse events (TRAEs) were reported in 94.0% of pts treated with ADA and 86.4% with DOCE; grade $3 TRAEs occurred in 47.0% and 45.7% of pts, respectively. TRAEs led to discontinuation of ADA in 7.7% of pts and DOCE in 14.3%. Additional efficacy and safety analyses, including subgroup analyses, will be presented.

Conclusions: In the phase 3 KRYSTAL-12 trial, ADA demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR over DOCE in pts with previously treated KRASG12C-mutated NSCLC. Safety profile of ADA was consistent with previous reports and with no new safety signals. These results further support ADA as an efficacious treatment option for pts with previously treated KRASG12C-mutated locally advanced or metastatic NSCLC.
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LBA8002

BEAT-meso: A randomized phase III study of bevacizumab (B) and standard chemotherapy (C) with or without atezolizumab (A), as first-line treatment (TX) for advanced pleural mesothelioma (PM)—Results from the ETOP 13-18 trial.

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Background: The currently approved frontline TXs for PM are the combination of ipilimumab/ nivolumab or platinum plus pemetrexed. The addition of B to C has been shown to improve overall survival in a randomized clinical trial. While combined immunotherapy or single agent immunotherapy with C is superior to C alone, there is potential for a synergistic triple combination of C, B, and immunotherapy.

Methods: BEAT-meso (NCT03762018) is an international open-label, 1:1 randomized phase III trial, stratified by histology and stage. The objective is to determine the efficacy and safety of adding A (1200 mg, Q3W until progression) to B (15mg/kg, Q3W until progression) and standard C (4-6 cycles of carboplatin AUC5 with pemetrexed 500 mg/m2 , Q3W), as first-line TX for advanced PM. The trial is designed to detect an increase in the median overall survival (OS, primary endpoint) with the addition of A, aiming for a hazard ratio (HR) of 0.708, at 2.5% 1-sided alpha and 82% power (284 deaths, sample size 400 patients (pts)). In the pre-specified interim efficacy analysis (80% of the events, 01/2023), boundary was not crossed, and the trial continued to completion. Secondary endpoints include progression-free survival (PFS), objective response rate (ORR), disease control rate, duration of response (DoR), adverse events (AEs) assessed by CTCAE v5.0 and symptom-specific and global quality of life (QoL).

Results: Between 04/2019 and 03/2022, a total of 400 pts was randomized, 200 per arm. The median age was 70 years, 79% were male, 50% were former smokers, 65% had ECOG performance status 1 and 78% had epithelioid histology. At a median follow-up of 35 months (m) (as of 1/09/2023), median OS was 20.5m [95% CI: 17.5-23.3] in the ABC and 18.1m [15.7-20.9] in the BC arm (deaths: 145 & 150; HRABC vs BC=0.84; [0.66 - 1.06], 2- sided stratified p=0.14, ITT final analysis). PFS was significantly longer in ABC with median 9.2m [8.1-10.9] vs 7.6m [6.9-8.3] in BC (HR=0.72; [0.59 - 0.89], 2-sided stratified p=0.0021). Histology shows a significant TX interaction for both PFS and OS. The OS HR is 0.51 [0.32-0.80] for non-epithelioid and 1.01 [0.77-1.32] for epithelioid (interaction p=0.012). In an exploratory analysis, post-progression OS was significantly different between the two arms, adjusted for post-progression TX (HR=0.76; [0.58 - 0.99]). The ORR was 55% in ABC and 49% in BC (p=0.27), while median DoR was 8.2m [6.8-9.7] in ABC and 5.6m [4.8-7.0] in BC (p=0.0041). Global QoL change was not significantly different between the two arms. Grade3 TX-related AEs occurred in 55% of pts in ABC and 47% of pts in BC (grade 5: 7 and 1 pt, respectively).

Conclusions: The significant increase in median PFS with the addition of A did not translate into a significant increase in median OS. ABC demonstrated superiority over BC in nonepithelioid cases. Clinical trial information: NCT03762018. Research Sponsor: ETOP IBCSG Partners Foundation; MO40388.

LBA1

Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (ESOPEC trial).

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Background: The most effective multimodal approach for treatment of resectable locally advanced esophageal adenocarcinoma (EAC) is under debate. A prior ranking question is if neoadjuvant chemoradiation therapy or perioperative chemotherapy is superior. ESOPEC (NCT02509286) is a multicenter prospective randomized trial comparing neoadjuvant CROSS (41.4Gy plus carboplatin/paclitaxel) followed by surgery versus perioperative FLOT (5-FU/ leucovorin/oxaliplatin/docetaxel) and surgery for the curative treatment of EAC.

Methods: Patients with cT1 cN+ cM0 or cT2-4a cNany cM0 resectable EAC were eligible. The primary endpoint is overall survival (OS; 90% power; hazard ratio [HR] 0.645, 218 events needed; one sided significance level of 2.5%). Analysis is by intention-to-treat in all randomized patients. The effect of treatment on OS is estimated using Cox regression stratified by study site, and including N stage (N0, N+), and age as covariates.

Results: Between Feb 2016 and Apr 2020, 438 patients from 25 sites in Germany were randomly assigned to two treatment groups (221 FLOT; 217 CROSS). Baseline characteristics (male sex 89.3%, median age 63 [range 30-86], cT 3/4 80.5%; cN+ 79.7%) were well balanced between both arms. Neoadjuvant treatment was started in 403 patients (207 FLOT; 196 CROSS). Surgery was done in 371 patients (191 FLOT; 180 CROSS). R0 resection was achieved in 351 patients (180 FLOT; 171 CROSS). 90 days postsurgical mortality was 4.3% (3.2% FLOT; 5.6% CROSS). After a median follow up of 55 months, 218 patients had died (97 FLOT; 121 CROSS). Median OS was 66 (95% CI 36 – not estimable) months in the FLOT arm, and 37 (95% CI 28 – 43) months in the CROSS arm. The 3-year OS rates were 57.4% (95% CI 50.1 – 64.0%) for FLOT and 50.7% (95% CI 43.5 – 57.5%) for CROSS (HR 0.70, 95% CI 0.53- 0.92, p=0.012). In 359 patients with available tumor regression status, pathological complete response was achieved in 35 (19.3%, 95%-CI 13.9 – 25.9%) in FLOT and in 24 (13.5%, 95%-CI 8.8 – 19.4%) in CROSS.

Conclusions: Perioperative FLOT improves survival in resectable EAC compared to neoadjuvant CROSS. Funding: The trial was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation), project number 264590883. Clinical trial information: NCT02509286. Research Sponsor: DFG.

4005

NRG Oncology/RTOG 0848: Results after adjuvant chemotherapy +/- chemoradiation for patients with resected periampullary pancreatic adenocarcinoma (PA).

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Background: If 5FU/Capecitabine sensitized radiotherapy (RT) is beneficial in the adjuvant (adj) management of PA after adj chemotherapy (chemo) is controversial. NRG/RTOG 0848 was designed to address this issue.

Methods: This was a 2 step NCTN randomized (rndmzd) trial. Step 1 rndmzd patients (pts) to 5 cycles of gemcitabine +/- Erlotinib. Step 2 rndmzd pts to a 6th cycle of the same chemo +/- 5FU/Capecitabine with 50.4 Gy in 28 fractions RT (chemo+CRT). Step 1 eligibility included: R0/R1 resection, M0, ECOG PS 0-1, CA19-9#180. Step 2 eligibility included . 4 cycles chemo (gem, gem combo, (m)FOLFIRINOX). RT included real time 3D/IMRT treatment (RX) plan review, scoring, and approval. At Step 2, pts stratified by nodal status (+ vs -), CA19-9 (#90 vs . 90-180), surgical margins (R0 vs R1), and adjuvant chemo. Primary endpoint was OS. Secondary endpoints are DFS and AEs (CTCAEv4). Assuming 17 months median OS (chemo) and hypothesized 22.5 months (chemo+CRT), sample size was 354 pts (HR = 0.76, 80% power, 1-sided a = 0.05, 316 OS events). Due to lower than projected event rate, trial was amended to report at the earlier of (a) 316 observed OS events or (b) 5 years of follow-up time from Step 2 accrual closure (265 OS events, 72% power, same a). OS and DFS were estimated by Kaplan-Meier and arms compared using log-rank test. Multivariable analyses (MVA) used Cox proportional hazards models.

Results: Accrual began 11/2009; closed 10/2018. 354 pts rndmzd (174 chemo, 180 chemo+CRT). Median follow-up for all & alive pts = 2 & 7 years, respectively, with 270 OS events. Median age 63, 45% female, 81% white, 13% AA. 83% R 0, 26% node negative, 96% CA19-9 , 90. 13% of chemo+CRT pts did not receive RT. AEs were comparable (grade 4: 10% [chemo] vs 11% [chemo+CRT] and 1 grade 5 AE in each arm). Univariate OS/DFS results shown in Table. In initial MVA, RX, CA19-9, surgical margins were not statistically significantly associated with OS or DFS, but nodal status (OS, DFS) and race (OS) were. In further analyses, significant interactions were found between RX and nodal status for both OS and DFS. Node negative pts treated with chemo+CRT had better outcome than chemo pts; node positive pts did not (Table).

Conclusions: Chemo+CRT did not improve OS overall, but did improve DFS. Both OS and DFS were improved with Chemo+CRT in node negative pts. Chemo+CRT did not increase Gr 4 or 5 AEs compared to chemo. Clinical trial information: NCT01013649. Research Sponsor: None

LBA1001

Abemaciclib plus fulvestrant vs fulvestrant alone for HR+, HER2- advanced breast cancer following progression on a prior CDK4/6 inhibitor plus endocrine therapy: Primary outcome of the phase 3postMONARCH trial.

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Background: The combination of CDK4/6 inhibitors (CDK4/6i) + endocrine therapy (ET) is the standard first line treatment for HR+, HER2- advanced breast cancer (ABC). While disease progression occurs in nearly all patients (pts) with ABC, the optimal treatment for pts who experience progression on a CDK4/6i + ET remains uncertain. Real-world evidence suggests that use of abemaciclib after disease progression on a prior CDK4/6i prolongs progression-free survival (PFS) in ABC; however, Phase 2 trials with other CDK4/6i have generated mixed results. Here we present the primary outcome analysis for the Phase 3 postMONARCH trial (NCT05169567) of fulvestrant + abemaciclib or placebo in pts with HR+, HER2- ABC following disease progression on prior CDK4/6i + ET.

Methods: postMONARCH was a global, doubleblind, placebo-controlled study with pts randomized 1:1 to abemaciclib + fulvestrant or placebo + fulvestrant. Eligible pts had disease progression on a CDK4/6i + AI as initial therapy for ABC or relapse on/after a CDK4/6i + ET as adjuvant therapy for early breast cancer. No other prior treatment for ABC was permitted. Primary endpoint was investigator-assessed PFS; secondary endpoints included PFS by blinded independent central review (BICR), overall survival (OS), objective response rate (ORR), and safety. Assuming a hazard ratio (HR) of 0.7, the study had ~80% power to detect superiority for abemaciclib, with a cumulative 2-sided type I error of 0.05. Kaplan-Meier method was used to estimate PFS curves and treatment effect was estimated using a stratified Cox proportional hazard model.

Results: A total of 368 pts were randomized to abemaciclib + fulvestrant (n = 182) or placebo + fulvestrant (n= 186). Most pts (99%) enrolled directly after CDK4/6i + ET as initial therapy for ABC. Prior CDK4/6i was 59% palbociclib, 33% ribociclib, and 8% abemaciclib. At interim analysis, the study reached the prespecified criteria for significantly improved investigator-assessed PFS with abemaciclib + fulvestrant compared to placebo + fulvestrant (169 events, HR = 0.66; 95% CI 0.48 – 0.91; p = 0.01). At primary analysis (258 events), the HR was 0.73 (95% CI 0.57 – 0.95), with PFS rates at 6 months of 50% vs 37% for the abemaciclib and placebo arms, respectively. Consistent effect was seen across major clinical and genomic subgroups, including pts with baseline ESR1 or PIK3CA mutations. ORR was improved with abemaciclib compared to placebo (17% vs 7%, respectively, in pts with measurable disease). PFS according to BICR was also improved with HR = 0.55 (95% CI 0.39 - 0.77). OS remains immature (20.9% event rate). Safety was consistent with the known profile of abemaciclib.

Conclusions: Abemaciclib + fulvestrant demonstrated statistically significant PFS improvement in pts with ABC progression on prior CDK4/6icontaining therapy. Clinical trial information: NCT05169567. Research Sponsor: Eli Lilly and Company.

LBA1000

Trastuzumab deruxtecan (T-DXd) vs physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06).

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Background: T-DXd is approved for HER2-low (IHC 1+ or 2+/ISH-negative) mBC after $1 line of chemotherapy (CT). DB-06 (NCT04494425) evaluated T-DXd in pts with HER2-low or -ultralow (IHC 0 with membrane staining), HR+ mBC after disease progression (PD) on endocrine-based therapy and no prior CT for mBC.

Methods: Pts with HER2-low or -ultralow, HR+ mBC were randomized 1:1 to TDXd 5.4 mg/kg or TPC. Pts had no prior CT for mBC, with $2 lines of ET for mBC, or 1 line of ET for mBC if PD occurred #24 months (mo) of adjuvant ET or #6 mo of ET+CDK4/6i for mBC. Primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR) in HER2-low. Key secondary endpoints were PFS in intent-to-treat (ITT = HER2-low and -ultralow) and overall survival (OS). Other endpoints included objective response rate (ORR) and safety.

Results: As of Mar 18, 2024, 866 pts (HER2-low, n=713; HER2-ultralow, n=153) were randomized; 90.4% had prior CDK4/6i. TPC group pts were selected for capecitabine (59.8%), nab-paclitaxel (24.4%) or paclitaxel (15.8%). TDXd significantly improved PFS vs TPC in HER2-low (HR, 0.62 [95% CI 0.51, 0.74], P,0.0001; median, 13.2 vs 8.1 mo). ITT and HER2-ultralow results were consistent with HER2-low (Table). Median treatment duration was 11.0 mo (T-DXd) vs 5.6 mo (TPC). OS was immature at first interim analysis (HER2-low HR, 0.83 [95% CI 0.66, 1.05], P=0.1181; median follow up, 18.6 mo). Grade (Gr) $3 drugrelated adverse events occurred in 40.6% (T-DXd) vs 31.4% (TPC). Adjudicated interstitial lung disease / pneumonitis occurred in 49 (11.3%; 0.7% Gr 3/4, 0.7% Gr 5) vs 1 (0.2% Gr 2) pts receiving TDXd vs TPC.

Conclusions: T-DXd showed a statistically significant and clinically meaningful PFS benefit vs TPC (CT) in HER2-low mBC. HER2-ultralow results were consistent with HER2-low. Safety was in line with known profiles. DB-06 establishes T-DXd as a standard of care following $1 endocrine-based therapy for pts with HER2-low and -ultralow, HR+ mBC. Clinical trial information: NCT04494425. Research Sponsor: This study is sponsored by AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).

LBA500

A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.

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Background: Prognosis of pts with early triple negative breast cancer (TNBC) is still poor and new effective treatments are needed. TNBC is the most immunogenic BC subtype, and this may account for sensitivity to immune checkpoint inhibitors. The A-BRAVE trial was designed to evaluate the efficacy of avelumab, an anti PD-L1 antibody, as adjuvant treatment for pts with early TNBC at high risk.

Methods: This is a phase III, multicentric, randomized adjuvant study comparing 1 year of treatment with the anti PD-L1 avelumab vs observation for TNBC pts considered at high risk of relapse. Pts were enrolled after they completed standard treatment with curative intent including surgery and neoadjuvant/adjuvant chemotherapy. High risk was defined as: 1) invasive residual disease (breast and/or nodes) after neoadjuvant chemotherapy (Stratum A), 2) .pN2/any pT, pN1/pT2, or pN0/pT3 after primary surgery (Stratum B). Pts were randomly assigned (1:1, balanced for strata A and B) to Avelumab 10 mg/kg I.V. q2w for 1 year or observation. Co-primary endpoints were disease free survival (DFS) in the total population and in Stratum A. 474 pts were needed to detect, in the total population, an improvement from 60% to 73.6% 3-year DFS rate (HR 0.6; 90% power, 1-sided test, alfa 2%). 172 DFS events were required to perform the event-driven analysis. Assuming a proportion of 70-80% pts enrolled in Stratum A, the expected power to detect an HR 0.6 at alpha allocated in this subgroup is 70- 79%. Overall survival was a secondary endpoint.

Results: From June 2016 to October 2020, 477 pts were randomly assigned from 64 Italian and 6 UK centers. 11 pts (3 avelumab, 8 control) withdrew consent immediately after randomisation and are excluded from further analyses. 378 pts entered Stratum A (83%), of whom 99 (57 avelumab, 42 control) received further chemotherapy after surgery prior to enrollment in the trial. Efficacy results for the two coprimary DFS endpoints and the secondary OS endpoints are reported in the table.

Conclusions: One year adjuvant avelumab versus control does not significantly improve DFS in high-risk TNBC patients. Nevertheless, the secondary enpoind OS was significanlty improved with avelumab vs control. RFS and DMFS will also be reported. A centralised collection of tumor tissue, plasma and feces has been performed and will allow a number of correlative studies. Clinical trial information: NCT02926196. Research Sponsor: Merck KGaA.

LBA502

A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial.

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Background: Triple-negative breast cancer (TNBC) is known for its high risk of early relapse and poor prognosis. Platinum agents have shown to increase pathological complete response (pCR) rates when added to neoadjuvant chemotherapy for TNBC. However, evidence regarding the survival benefit of platinum in this setting remains inconclusive. The PEARLY trial is a multicenter, randomized, open-label, phase 3 study designed to assess the efficacy and safety of carboplatin in combination with anthracycline/taxane therapy compared to standard anthracycline/taxane alone as either neoadjuvant or adjuvant treatment in early-stage TNBC.

Methods: Patients with stage II or III TNBC were randomly assigned to either the carboplatin arm or the standard therapy arm, stratified by nodal status, institution, treatment setting (neoadjuvant vs adjuvant), and germline BRCA status. The standard therapy involved doxorubicin and cyclophosphamide (AC) followed by taxane treatment. The experimental arm included carboplatin in addition to taxane following AC. The primary endpoint was eventfree survival (EFS), defined as disease progression or inoperable status for neoadjuvant therapy group, local or distant recurrence, occurrence of a second primary cancer, or death from any cause, while secondary endpoints encompassed overall survival (OS), invasive disease-free survival (IDFS), distant recurrence-free survival (DRFS), pCR rate, and safety. With a planned enrollment of 878 patients, the trial aimed for 80% power to detect a hazard ratio of 0.70 for EFS at a two-sided alpha level of 0.05, anticipating 248 EFS events over a 5-year follow-up period.

Results: Between Jan 2016 and Jun 2020, 868 patients across 22 institutions in South Korea were enrolled. At a median follow-up of 51.1 months, carboplatin significantly improved EFS compared to the control arm (hazard ratio [HR], 0.68; 95% confidence interval [CI]: 0.50 to 0.93; p=0.017). The 5-year EFS rates were increased from 74.4% to 81.9%, demonstrating a 7.5% difference. Subgroup analysis showed consistent benefits across various patient categories. Secondary endpoints like IDFS and DRFS also favored carboplatin arm. OS data were immature, a total of 43 patients (10.2%) in the carboplatin arm and 57 patients (13.1%) in the control arm died (HR 0.66; 95% CI: 0.42 to 1.01). Grade $3 treatment-related adverse event rates were 74.6% (1 death due to infection) in the carboplatin arm and 56.7% (2 deaths due to infection and suicide) in the control arm.

Conclusions: The addition of carboplatin to standard anthracycline followed by taxane therapy significantly improved EFS in patients with earlystage TNBC. The safety profile was consistent with the known expectations for each regimen. Clinical trial information: NCT02441933. Research Sponsor: Boryung; Hanmi; GC Corp.; Samyang Biopharm; Faculty research grant of Yonsei University College of Medicine for 2014 (6-2014-0188).

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