emtansine, trastuzumab-deruxtecan, and lapatinib. Primary outcome was overall survival (OS). RESULTS: Of 7780 abstracts screened, 91 publications and a total of 109 patients were included in the final analysis. Patients receiving chemotherapy (either IT, IV, or as part of an antibody-drug conjugate) concurrently with HER2-TT (N=57) exhibited a median OS (mOS) of 44.0 months, compared to patients treated with targeted anti-HER2 therapies alone (N=52), which exhibited a mOS of 14.5 months (P=0.009, hazard ratio (HR): 0.538, 95% confidence interval (CI): 0.328-0.883). Patients receiving IT trastuzumab (N=83) exhibited a median progression-free survival (mPFS) and mOS of 6.0 and 21.0 months, respectively, while patients receiving IV trastuzumab (N=14) exhibited a mPFS and mOS of 6.5 and 27.0 months, respectively (PFS: P=0.31, HR: 0.712, 95% CI: 0.331-1.531; OS: P=0.68, HR: 1.154, 95% CI: 0.587-2.266). In the subgroup of patients receiving IT trastuzumab (N=58), those who concurrently received IT chemotherapy (N=48) exhibited mPFS and mOS of 5.7 and 14.0 months, respectively, while patients concurrently receiving IV chemotherapy (N=10) exhibited a mPFS and mOS of 6.0 and 27.0 months, respectively (PFS: P=0.45, HR: 1.360, 95% CI: 0.602-3.073; OS P=0.29, HR: 1.821, 95% CI: 0.630-5.260). CONCLUSIONS: HER2-TT is an effective therapeutic strategy for BCLM. Patients with BCLM receiving concurrent cytotoxic chemotherapy alongside HER2-TT experience prolonged mOS. IV and IT trastuzumab are similarly effective. Univariate and multivariate analyses will be presented.

SYST-06

INTRACRANIAL ACTIVITY OF TEPOTINIB IN PATIENTS WITH *MET* EXON 14 (*MET*EX14) SKIPPING NSCLC ENROLLED IN VISION

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BACKGROUND: Brain metastases (BMs) occur in 20–40% of patients with *MET*ex14 skipping NSCLC. Tepotinib, a highly selective MET inhibitor, demonstrated an objective response rate (ORR) of 49.1% and median duration of response (mDOR) of 13.8 months, in *MET*ex14 skipping NSCLC patients in the Phase II VISION study (Cohorts A+C; N=275). Here, we report the intracranial activity of tepotinib in VISION. METHODS: Patients with *MET*ex14 skipping NSCLC received oral tepotinib 500 mg QD (450 mg active moiety). Patients with BM (asymptomatic and symptomatic/stable) were eligible. Primary endpoint was systemic ORR (RECIST v1.1); a subgroup analysis in patients with BM was predefined (data cut-off: February 1, 2021). An *ad-hoc* retrospective analysis of brain lesions was conducted by an IRC using RANO-BM criteria. Responses were determined in patients with ≥1 evaluable post-baseline tumor assessment. For those with only non-target lesions (NTLs) per RANO-BM (enhancing and non-enhancing NTLs), disease control was defined as non-complete response (CR)/nonprogressive disease (PD). Data cut-off: July 1, 2020. RESULTS: Fifty-one patients had baseline BM (Cohorts A+C). Systemic efficacy was consistent with the overall population (ORR 52.9% [95% CI: 38.5, 67.1], mDOR 9.0 months [95% CI: 5.6, not estimable]). Fifteen patients were evaluable by RANO-BM (Cohort A); 12 received prior radiotherapy for BM (median 6.4 weeks before treatment). Systemic best objective responses (BORs) were partial response (PR, n=9), stable disease (SD, n=3), and PD (n=3). Seven patients had target CNS lesions per RANO-BM (all with prior radiotherapy); intracranial BORs were PR (n=5), SD (n=1), and PD (n=1). For patients with NTL only (n=8), one had PD, and seven achieved intracranial disease control with three patients achieving CR of the enhancing NTL. 13/15 patients achieved intracranial disease control. CONCLUSIONS: Tepotinib demonstrated robust systemic activity in patients with *MET*ex14 skipping NSCLC with BM, complemented by intracranial activity in an ad-hoc analysis using RANO-BM.

SYST-07

WINDOW-OF-OPPORTUNITY STUDY OF ONC201 IN PEDIATRIC PATIENTS WITH DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG) AND THALAMIC GLIOMA

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BACKGROUND: H3 K27M-mutant diffuse midline glioma is a universally fatal malignancy primarily affecting children and young adults; no effective systemic therapy is available. ONC201, a first-in-class imipridone, is an oral, blood-brain barrier penetrating, selective small molecule antagonist of dopamine receptor D2/3 and agonist of the mitochondrial protease ClpP. ONC201 monotherapy demonstrated durable objective responses in adults with recurrent H3 K27M-mutant glioma. This phase 1 trial will evaluate ONC201±radiotherapy (RT) in pediatric patients with H3 K27M-mutant midline glioma DIPG. METHODS: This multicenter, open-label, dose escalation and expansion phase 1 study of ONC201 is comprised of eight arms that will evaluate the recommended phase 2 dose (RP2D) of ONC201, biomarkers, and pharmacokinetics (PK) of ONC201±RT in various treatment settings (NCT03416530). Arm G previously defined the RP2D for twice-weekly ONC201 on consecutive days. Arm H, for which enrollment is ongoing, will estimate the influence of tumor location and blood-brain barrier integrity on PK and intratumoral ONC201 exposure in biopsy-eligible pediatric tumors (DIPG or contrast-enhancing thalamic glioma). Patients eligible for Arm H will be aged 2-≤19 years, ≥2 weeks from last RT administration, and have a KPS/LPS ≥50; prior confirmation of H3 K27M mutation is not required. In Arm H, single-agent ONC201 administration will occur twice-weekly on consecutive days during each 21-day cycle at the RP2D defined in Arm G. Arm H has a planned enrollment of 27 patients (DIPG, n=15; thalamic glioma, n=12), with three patients undergoing a single biopsy at each of the following time points: 1-3 h post-first dose, 22-26 h post-second dose, 1-3 h post-first dose, 6-10 h post-second dose, and 22-26 h post-second dose. The 22-26 h post-first dose biopsy in thalamic glioma was previously collected and will not be assessed in this treatment arm. Plasma for PK analysis will be collected from all patients.

SYST-08

SURVIVAL ANALYSIS OF METASTATIC MELANOMA PATIENTS WITH BRAIN METASTASIS USING SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER)

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INTRODUCTION: Melanoma brain metastases (BM) are common and are historically associated with poor prognosis. In the early 2010s, the treatment paradigm for malignant metastatic melanoma shifted with the introduction of immunotherapy (IT). Recent studies suggest that IT provides survival benefits for patients with BM from melanoma primary. The goal of this study was to validate these findings in a large population cohort. METHODS: Data were collected from the Surveillance, Epidemiology and End Results (SEER) database, version 8.3.4 (22 March 2017). Three cohorts were created based on the FDA approval date of IT: ipilimumab (2011), nivolumab (2014), and nivolumab plus ipilimumab (2015) for use in metastatic melanomas. Respectively, the cohorts are defined as the pre-IT era cohort (2010), early-IT era cohort (2011-2015) and late-IT era cohort (2016-2018). One-year overall survival (OS), 2-year OS, and median OS were assessed using a Kaplan-Meier analysis and log rank tests. RESULTS: