Results: As of 01 Dec 2019, of 300 enrolled pts, 70 had received tislelizumab for >12 mo (median age, 54 yr; ≥2 lines of prior systemic therapy, 49%). Median duration of treatment was 20.9 mo with 29 pts treated beyond progression. The most common tumor types of pts with LTE were NSCLC (n=16) and NPC (n=8). For all pts with LTE, ORR was 55.7%, with responses observed in both PD-L1 >10% and <10% pts (Table). With a median study follow-up of 24.7 mo, median duration of response and median OS were not reached. Commonly reported treatment-related adverse events (TRAEs) included increased ALT (n=22, 31.4%) and AST (n=22, 31.4%); TRAEs across the entire study were mostly of grade ≤2 severity. Three pts (4.3%) had TRAEs leading to treatment discontinuation; no pt reported a TRAE leading to death.

Conclusions: Tislelizumab remained generally well tolerated with no new safety signals when administered for >12 mo and elicited durable responses in pts with a variety of tumor types, regardless of PD-L1 status.

Clinical trial identification: NCT04068519.

Editorial acknowledgement: Writing and editorial assistance was provided by Stephanie Lindsey, and Elizabeth Hermans, PhD (OPEN Health Medical Communications, Chicago, IL), and funded by the study sponsor.

Legal entity responsible for the study: Beigene, Ltd.

Funding: Beigene, Ltd.

Disclosure: L. Shen: Full/Part-time employment: Beigene, Ltd.; Y. Wu: Honoraria (self), Advisory/Consultancy; AstraZeneca; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Boehringer Ingleheim; Honoraria (self): Lilly, Honoraria (self): Pfizer; Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Roche; Honoraria (self): Sanofi; Advisory/Consultancy; Novartis; Advisory/Consultancy; Pfizer; Advisory/Consultancy; Bayer; Advisory/Consultancy; Novartis; Advisory/Consultancy; Simcere; Advisory/Consultancy; Shanghai Junshi Biosciences; Advisory/Consultancy: Ointgene; Advisory/Consultancy: Betta Pharmaceuticals Co., Ltd.. All other authors have declared no conflicts of interest.

Table: 552P

<table>
<thead>
<tr>
<th>Best overall response in patients with long-term exposure (&gt;12 Months) to tislelizumab by PD-L1 status</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 ≥10% (n=18)</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>CR, n (%)</td>
</tr>
<tr>
<td>PR, n (%)</td>
</tr>
<tr>
<td>SD, n (%)</td>
</tr>
<tr>
<td>PD, n (%)</td>
</tr>
<tr>
<td>ORR, %</td>
</tr>
</tbody>
</table>

Abbreviations: CI, Confidence interval; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Background: NCI-MATCH assigned patients (pts) with advanced cancer and progression on prior treatment to targeted therapies, based on genomic alterations in pre-treatment tumour tissue. Arm J evaluated the combination of trastuzumab/pertuzumab (HP) across HER-2 amplified tumours.

Methods: Eligible pts had HER2 amplification (copy number [CN] ≥7) detected by central next generation sequencing (NGS) or through NCI designated laboratories. Pts with breast/gastroesophageal adenocarcinomas were then stratified to HP arm if they had deleterious PIK3CA mutations. Pts with breast/gastroesophageal adenocarcinomas, and those with HER2-directed therapy were excluded. Enrollment of pts with colorectal cancer was capped at 4 based on emerging data. Pts received HP IV q3 weeks until disease progression or unacceptable toxicity, with restaging q3 cycles. Primary endpoint was objective response rate (ORR) of enrollment; an apriori 92% power to distinguish ORR of 25% from a null of 5%, with one-sided type 1 error of 1.8%. Secondary endpoints included progression-free survival (PFS), 6-month PFS, and overall survival (OS). Data cut was 8-FEB-2020.

Results: 35 pts were enrolled 3/2017-6/2019; 2 were ineligible. Tumour types included: gynecologic (n=14), hepatobiliary (10), colorectal (4), urothelial (3), esophageal squamous, and salivary gland (1 each). 58% were women, and 79% Caucasian. Median age was 64 (range 31-83), and 51% had ≥3 prior therapies (range 1-11). Median cycles received was 3 (1-20). Of 33 treated, 24 had CN ≥7 confirmed by central lab (median CN=28). The confirmed ORR was 8.3% (2/24 partial responses [colorctal and cholangiocarcinoma], 90% CI 1.5-24%). There was one additional unconfirmed partial response (PR, urothelial cancer). Median PFS was 3.3 months (90% CI 2.0 - 4.6), 6-month PFS 23.3% (90% CI 13.6 – 40.1) and median OS 8.1 months (90% CI 5.5 - 12.4). Treatment-emergent adverse events were consistent with prior HP studies. There was no association between HER2 CN and response.

Conclusions: HP had activity in a minority of tumours in this population, but did not meet the predefined efficacy benchmark for non-breast/gastroesophageal cancers with HER2 amplifications by NGS. Translational studies will focus on mechanisms of response and resistance.

Clinical trial identification: NCT02465060.

Legal entity responsible for the study: ECOG-ACRIN.
Selinexor in combination with carboplatin and paclitaxel in patients with advanced or metastatic solid tumours: Results of an open label, single-center, multi-arm phase Ib study


Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background: Selinexor is a first-in-class novel, oral potent selective inhibitor of nuclear export which blocks the transport protein called Exportin-1. Carboplatin+ Taxol (CT) is one of the standard chemotherapy regimens used in various tumour types. Preclinical models have suggested that selinexor and CT exert antitumor activity in multiple malignancies.

Methods: This was an open label, single-center, multi-arm phase Ib study utilizing a “3 + 3” design and a “basket type” expansion. CT + selinexor was employed as one of the 13 parallel arms. Patients with advanced or metastatic solid tumours who were unresponsive or had relapsed following prior systemic therapy or where the addition of selinexor to standard chemotherapy deemed appropriate and acceptable, were eligible.

Results: Of 13 patients treated, 12 patients were evaluable for response. The most common cancers were breast (n=4), esophageal (n=2), ovarian (n=2) and non-small cell lung cancers (n=2). All 13 patients had at least one treatment-emergent adverse events (TEAE) and the commonest TEAE were anemia (84%), neutropenia (84%), leukopenia (84%), thrombocytopenia (84%), fatigue (61%), elevated AST or ALT (61%), nausea (53%), hypomagnesemia (53%), and peripheral motor or sensory neuropathy (53%). The most prevalent grade ≥ 3 TEAE were neutropenia (69%), thrombocytopenia (53%), leukopenia (46%), and anemia (15%). One patient at 60mg once weekly had experienced DLT with grade 4 neutropenia lasting >7 days. Partial response was noted in 4 patients (33.3%) in patients with esophageal (n=2), 1 patient each with breast and ovarian cancer. Five patients (41.7%) achieved stable disease and the clinical benefit rate was 75%. Majority of patients (84%), including 3 patients who had PR, had prior exposure to carboplatin and/or paclitaxel. Treatment time to failure (TTF) ranged from 10 to 148 weeks and TTF for patients with PR was from 18 to 23 weeks.

Conclusions: Oral selinexor can be safely combined with CT and the RP2D was 60 mg once weekly in combination with CT. The combination conferred appreciable clinical activity with durable objective responses which should further be explored in tumour types for which CT is used as standard of care.

Clinical trial identification: NCT02419495.

Legal entity responsible for the study: UNICANCER.

Funding: AstraZeneca.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.669

SS5P Metronomic oral vinorelbine (MOV) combined with tremelimumab (T) + durvalumab (D) in advanced solid tumours (AST): Dose finding results

A. Gonzalves1, T. de La Motte Rouge2, A. Bruno3, N. Isambert1, A. Hervieu1, P. Legrand1, C. Cropet1

1Medical Oncology Department, Institute Paoli Calmettes, Marseille, France; 2Medical Oncology, Centre Eugène – Marquis, Rennes, France; 3Unité de Phases Précoces / Oncologie Médicale, Centre Georges-François Leclerc, Dijon, France; 4R&D, UNI-CANCER, Paris, France; 5Direction de la Recherche Clinique et de l’Innovation (DRCI), Centre Léon Bérard, Lyon, France

Background: Anti-PD1/PD-L1 agents have only moderate antitumour activity in some AST, including breast (BC), prostate (PC), cervical (CC) and head and neck (HNC) cancers. Combining anti-PD-L1 with anti-CTLA4 therapies (such as D and T, respectively) may significantly improve efficacy. Metronomic chemotherapy may have pro-immune effects. MOV is an ongoing, open-label, single arm phase 1/2 study examining the combination of T+D with MOV in AST patients.

Methods: Patients [pts] with BC, CC, HNC, PC and miscellaneous cancers with high tumour mutational burden (ntMB) were eligible in case of advanced disease resistant to conventional therapies. 2 was administered IV, 75 mg Q4W, for up to 4 cycles and D was administered IV, 1500 mg Q4W, for up to 26 cycles (or 24 months whichever is longer). MOV was administered orally thrice weekly until disease progression and up to 3 dose levels (DL) were to be investigated (DL1=30 mg, DL2=40 mg and DL3=20 mg). The primary objective of the phase 1 part of the study was to determine the maximum tolerated dose (MTD) and the recommended dose for phase II (RP2D) in MOV in combination with T+D. The primary objective was the occurrence of Dose Limiting Toxicities (DLTs) on cycle 1. Secondary objectives included safety, clinical benefit rate, overall response rate, duration of response and progression-free survival.

Results: In total, 14 pts (13 female and 1 male) were enrolled in the phase I part of the study, this incuded BC (n=9), CC (n=2), HNC (n=2) and PC (n=1). The median age was 55 (range=32-76). Twelve pts were evaluable for the dose escalation part. No DLT was observed in the first 3 pts treated and they were evaluable at DL1 and DL2. An extension cohort of 6 pts was included at DL2 in order to confirm the RP2D and 1 DLT was observed (neutropenia with fever, grade 4). Accordingly, DL2 was selected as the RP2D. Two (14.3%), 4 (28.6%) and 4 (28.6%) pts had grade [G] 3 or higher adverse events (AEs) related to MOV, D and T, respectively. Immune-related AEs included colitis (1G2, 1G3), rash (2G1, 2G3), and thyroiditis (2G1, 3G2). No toxic deaths were recorded. One pt (CC) had a complete response. Phase II is ongoing with promising results in BC and CC cohorts.

Conclusions: MOV 40 mg thrice weekly is the RP2D in combination with T+D. The safety profile of the combination is consistent with previous reports of T+D combination or MOV.

Clinical trial identification: NCT03518606.

Legal entity responsible for the study: UNICANCER.

Funding: AstraZeneca, Pierre Fabre.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.669

SS5P Initial clinical experience of lucitanib + nivolumab in advanced metastatic solid tumours: Data from the phase Ib/II LIO-1 study (CO-3810-101; NCT04042116)


1Medical Oncology, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; 2Florida Cancer Specialists, Sarah Cannon Research Institute, Sarasota, FL, USA; 3Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; 4Biostatistics, Clovis Oncology, Inc., Boulder, CO, USA; 5Clinical Development, Clovis Oncology, Inc., Boulder, CO, USA; 6Translational Medicine, Clovis Oncology, Inc., Boulder, CO, USA; 7Clinical Pharmacology, Clovis Oncology, Inc., Boulder, CO, USA; 8Clinical Science, Clovis Oncology UK ltd., Cambridge, UK

Background: Proangiogenic factors contribute to immunosuppression in the tumour microenvironment. Inhibiting angiogenesis with a tyrosine kinase inhibitor (TKI) may attenuate these signals and improve immunotherapy efficacy. This study is investigating the safety and efficacy of the angiogenesis inhibitor lucitanib+nivolumab.

Methods: The phase Ia dose-escalation part of LIO-1 will determine the recommended phase II dose of lucitanib in combination with pembrolizumab (Luc+Pemb [L+P]) (40 mg IV once 42 weeks) in patients (pts) with an advanced refractory or progressive solid tumour and no satisfactory treatment options. The lucitanib dose has been evaluated at a once-daily dose of 6, 8 and 10 mg. Dose-limiting toxicities (DLTs) were assessed during the first 21 days of treatment. Tumour response was assessed by independent centralized RECIST v1.1. Steady-state pharmacokinetic (PK) evaluation was performed for lucitanib. Fresh tumour biopsies were collected prior to study entry for translational analysis of biomarkers such as tumour mutation burden, microsatellite instability and PD-L1 expression.

Results: As of 14 May 2020, 15 pts have been treated with 6 mg (n=7), 8 mg (n=5) or 10 mg (n=3) lucitanib in combination with nivolumab. In the first cohort of 4 pts evaluating 6 mg, 1 DLT (Grade [G]3 proteinuria) was observed, leading to