P-19 Subgroup analysis of the number of prior lines of systemic therapy and clinical outcomes associated with tislelizumab in patients with previously treated advanced hepatocellular carcinoma (HCC)

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Background: Tislelizumab, an anti-programmed cell death protein 1 (PD-1) monoclonal antibody, showed clinical activity and was well tolerated in patients with previously treated advanced HCC in the phase 2 RATIONALE-208 study (NCT03419897). This analysis examined the number of prior lines of systemic therapy and clinical outcomes associated with tislelizumab.

Methods: Patients who received ≥ 1 prior line of systemic therapy for advanced HCC, excluding immune checkpoint inhibitors, received tislelizumab 200 mg IV every 3 weeks. The primary endpoint was objective response rate by independent review committee (IRC) (ORR IRC) per RECIST version 1.1. Secondary endpoints included investigator-assessed (INV) ORR INV , duration of response by IRC (DoR IRC), DoR by INV (DoR INV), overall survival (OS), progression-free survival by IRC (PFS IRC), and safety.

Results: As of June 2021, 249 patients were enrolled; 138 had received 1 prior line of therapy and 111 patients had received ≥ 2 prior lines of therapy. Median (m) follow-up duration was 13.3 months and 11.9 months, respectively. Response rate assessed by IRC (1 prior line, ORR IRC =13.0% [95% CI: 7.9, 19.8]; ≥ 2 prior lines, ORR IRC =12.6% [95% CI: 7.1, 20.3]) and by INV (1 prior line, ORR INV =15.2% [95% CI: 9.7, 22.3]; ≥ 2 prior lines, ORR INV =13.5% [95% CI: 7.8, 21.3]) was generally consistent between subgroups. Number of prior lines of therapy did not impact OS (1 prior line, mOS=13.8 months [95% CI: 10.5, 19.1]; ≥ 2 prior lines, mOS=12.4 months [95% CI: 9.9, 15.2]) or PFS (1 prior line, mPFS IRC =2.6 months [95% CI: 1.4, 2.8]; ≥ 2 prior line, mPFS IRC =2.7 months [95% CI: 1.4, 2.8]). mDOR IRC was not reached in either subgroup. mDoR INV was not reached in the 1 prior line subgroup and was 14.6 months [95% CI: 7.6, 27.3] in the ≥ 2 prior lines subgroup. Treatment-emergent adverse events (TEAEs) were consistent between the 1 prior line and ≥ 2 prior lines subgroups; 94.2% vs 95.5% experienced any TEAE, 50.0% vs 48.6% experienced ≥ Grade 3 TEAEs, 38.4% vs 36.0% experienced serious TEAEs, 13.0% vs 9.0% experienced TEAEs that led to treatment discontinuation, 32.6% vs 30.6% experienced TEAEs that led to dose delay, and 11.6% vs 9.0% experienced TEAEs that led to death in the 1 prior line and ≥ 2 prior lines subgroups, respectively. Similarly, treatment-related adverse events (TRAEs) were consistent between the 1 prior line and ≥ 2 prior lines subgroups; 65.9% vs 60.4% experienced any TRAE, 17.4% vs 12.6% experienced ≥ Grade 3 TRAEs, 9.4% vs 4.5% serious TRAEs, 7.2% vs 2.7% experienced TRAEs that led to treatment discontinuation, 19.6% vs 17.1% experienced TRAEs that led to dose delay, and 0% vs 0% experienced TRAEs that led to death in the 1 prior line and ≥ 2 prior lines subgroups, respectively.

Conclusions: Effective second- and third-line treatment options are limited for patients with advanced HCC. This analysis indicates Tislelizumab is clinically active and well tolerated in patients with advanced HCC, regardless of the number (1 or ≥ 2) of prior lines of systemic therapy. Tislelizumab is being investigated further in a phase 3 study (NCT03412773).

Clinical trial identification: NCT03419897.

Editorial acknowledgement: This study is sponsored by BeiGene, Ltd. Medical writing support, under direction of the authors, was provided by Kirsty Millar, MSc, of Ashfield MedComms, an Ashfield Health company, and was funded by BeiGene, Ltd.

Legal entity responsible for the study: BeiGene, Ltd.

Funding: BeiGene, Ltd.

Disclosures: P. Merle: Advisory / Consultancy: Roche, BMS, AstraZeneca, Bayer, Eisai, MSD, Ipsen, Lilly, Genosciences; Research grant / Funding (self): Ipsen, Genosciences. J. Edeline: Advisory / Consultancy: Beigene; Research grant / Funding (institution): Beigene. L. Rimassa: Honoraria (self): Lecture fees: AbbVie, Amgen, Bayer, Eisai, Gilead, Incyte, Ipsen, Lilly, Merck Serono, Roche, Sanofi; Advisory / Consultancy: Amgen, ArQule, AstraZeneca, Basilea, Bayer, BMS, Celgene, Eisai, Exelixis, Genenta, Hengrui, Incyte, Ipsen, IQVIA, Lilly, MSD, Nerviano Medical Sciences, Roche, Sanofi, Servier, Taiho Oncology, Zymeworks; Research grant / Funding (institution): Agios, ARMO BioSciences, AstraZeneca, BeiGene, Eisai, Exelixis, Fibrogen, Incyte, Ipsen, Lilly, MSD, Nerviano Medical Sciences, Roche, Zymeworks. M. Bouattour: Honoraria (self): Bayer, Eisai, Roche; Advisory / Consultancy: Roche, IPSEN, Sirtex medical; Travel / Accommodation / Expenses: Astra-Zeneca, Roche, Bayer . B. Li: Shareholder / Stockholder / Stock options: BeiGene; Full / Part-time employment: BeiGene. S. Chica-Duque: Shareholder / Stockholder / Stock options: BeiGene. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.110

P-20 Predictors of distant relapse in rectal cancer patients submitted to preoperative chemoradiotherapy

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Background: Neoadjuvant chemoradiotherapy (nCRT) is the standard treatment for locally advanced rectal cancer. nCRT improves local control, however, this does not translate into a survival benefit. Long-term survival is mostly affected by the development of distant metastases after local treatments. This study aimed to evaluate predictive clinical factors for the development of early metastatic disease after nCRT.

Methods: All patients with stage II and III rectal adenocarcinoma, who underwent nCRT from January 2013 to December 2019 were identified. Serum measurements of Hemoglobin, C-Reactive Protein (CRP), platelets, ratio neutrophils/lymphocytes, CEA and CA 19.9 were obtained before nCRT. Patients were divided into two groups: those who developed distant relapse (Group A) and patients without distant relapse (Group B). For the comparison of the groups calculated by the threshold predictors value, the Chi-square test and the Fisher's exact test were used. Logistic regression was performed to determine univariate relationships and multivariate logistic regression analysis, adjusted for factors possibly related to distant disease relapse.

Results: The study included 162 patients. Most of the patients were male (n=103, 63.6%), the median age of the studied cohort was 63 years (interquartile range 18 years) and the ECOG 0 was predominant (n=132, 81.5%). At initial presentation and radiologic examination, most of the patients had cT3 disease (n=118, 72.8%) and 127 (35%) were node positive. Thirty-nine (24.1%) had distant relapse from neoadjuvant treatment and surgery (Group A) and 123 (75.9%) did not (Group B). A higher rate of distant relapse was associated with CEA levels above 2.2 ng/dL (p=0.002) and CPR above 8.8 mg/L (p=0.002). Multivariate analysis confirmed these factors to be independently correlated with a higher risk of metastasis, CEA 2.2 ng/dL (OR 0.061; 95% IC 0.005-0.695; p=0.024) and PCR 8.8 mg/L (OR 0.163; 95% IC 0.041-0.650; p=0.010).

Conclusions: High serum CEA and CPR may be associated with unfavorable early oncological outcomes after nCRT and surgery for rectal cancer. Defining unfavorable clinical characteristics may permit us to correctly drive the appropriate therapy to the right patient, possibly improving the current staging and thus hopefully outcomes.

Legal entity responsible for the study: The author.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.111

P-21 Molecular subtypes (profile) of colorectal cancer and their correlation with clinical and pathological profile in a tertiary care centre in India

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Background: Colorectal cancer is a heterogeneous disease with 3 molecular carcinogenesis pathways and 2 morphologic multistep pathways. The varied response rates to the standard therapeutic regimens is due to its heterogeneous tumor biology. A lot of the literature is from the western world on this molecular heterogeneity. We aimed to study the molecular subtypes of colorectal cancer and the correlation with clinical and pathological characteristics in Indian population.Objectives: To evaluate the clinical and pathological profile of colorectal cancers, to determine the frequency of molecular subtypes of colorectal cancers, to correlate between the molecular