2-1-2023

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LBA490 **Oral Abstract Session**

SWOG 1815: A phase III randomized trial of gemcitabine, cisplatin, and nab-paclitaxel versus gemcitabine and cisplatin in newly diagnosed, advanced biliary tract cancers.

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Background: Biliary tract cancers (BTCs) are a heterogeneous group of malignancies with a dismal prognosis. Gemcitabine-based regimens are the standard of care in advanced disease, but median overall survival (OS) is roughly 12 months. The addition of albumin-bound paclitaxel to gemcitabine and cisplatin (GAP) demonstrated promising efficacy in a 60 patient, single-arm phase II study (Shroff et al, JAMA Oncol 2019), with observed median OS of 19.2 months. **Methods:** SWOG 1815 is a randomized, open-label, phase III trial comparing GAP to gemcitabine/cisplatin (GC). The study included newly diagnosed advanced BTC patients (pts), randomized 2:1 to GAP vs. GC. GAP included gemcitabine at 800 mg/m2, cisplatin at 25 mg/m2 and albumin-bound paclitaxel at 100 mg/m2 on days 1 and 8 of a 21-day cycle. GC included standard dosing of gemcitabine at 1000 mg/m2 and cisplatin at 25 mg/m2 on days 1 and 8 of a 21-day cycle. Pts were treated until progression. The primary endpoint was overall survival (OS) with a target hazard ratio of 0.7 with 90% power and a 1-sided alpha of 0.025; randomization was stratified by disease site (intrahepatic cholangiocarcinoma [CCA] vs gallbladder adenocarcinoma [GBC] vs extrahepatic CCA), disease stage (locally advanced vs metastatic), and Zubrod PS 0 vs 1. **Results:** Of 441 eligible pts randomized, 55% were female. 67% of patients had intrahepatic CCA, 16% had GBC and 17% had extrahepatic CCA. Most pts had metastases (73%). Median OS with GAP vs. GC was 14 vs. 12.7 mo respectively (HR 0.93, 95% CI 0.74-1.19, p=0.58), ORR (confirmed and unconfirmed) 34% vs 25% (p=0.11) and median PFS 8.2 vs 6.4 mo (HR 0.92, 95% CI 0.72-1.16, p=0.47), respectively. Grade 3 and 4 treatment related adverse events (TRAEs) in $\geq$10% of pts for GAP and GC were anemia, neutropenia, and thrombocytopenia. GAP had more $\geq$ grade 3 hematologic AEs compared to the GC arm (60% vs. 45%, p=0.003). Discontinuation due to toxicity was at 24% vs 19% (p=0.26) with GAP vs GC. In exploratory subset analyses, GAP vs GC improved OS in pts with locally advanced disease (medians 19.2 vs 13.7 mo; HR 0.67, 95% CI 0.42-1.06, p=0.09) and in GBC pts (medians 17.0 vs 9.3 mo; HR 0.74, 95% CI 0.41-1.35, p=0.33). ORR for GAP vs GC in GBC was 50% vs 24% (p=0.09) and for locally advanced disease 28 vs 21% p=0.74. **Conclusions:** SWOG 1815 did not result in a statistically significant improvement in median OS with GAP vs. GC. The GAP regimen had higher rates of TRAEs without a statistically significant difference in discontinuation rates. Pts with locally advanced disease and GBC may benefit from the use of GAP. Further analyses are ongoing to understand potential benefit of GAP in subsets of BTC pts. Funding: NIH/National Cancer Institute grants CA180888, CA180819, CA180820, CA180821, and CA180868; and in part by Celgene Corporation, Summit, NJ (subsidiary of Bristol Myer Squibb). Clinical trial information: NCT#03768414. Research Sponsor: U.S. National Institutes of Health.