FPN# 6345 Bevacizumab plus Erlotinib as Switch Maintenance in Chemotherapy Responsive Advanced Biliary Tract Cancers (BEER-BTC): a multicentre, open-label, randomised, controlled, phase 2 trial

Dr. Vikas Ostwal1, Dr. Anant Ramaswamy1, Dr. Prabhat Bhargava1, Dr. Sujay Srinivas1, Dr. Akhil Kapoor2, Dr Bal Krishna Mishra2, Dr Anuj Gupta2, Sarika Mandavkar1, Sadhana Kannan1, Deepali Chaugule1, Rajshree Patil1, Manali Parulekar1, Dr. Chaitali Nashikkar1, Dr. Suman Kumar Ankathi1, Dr. Nitin Shetty1, Dr Rajiv Kumar Kaushal1

1Tata Memorial Hospital (HBNI), Mumbai, India; 2Homi Bhabha Cancer Hospital, Varanasi, Varanasi, India

BACKGROUND

• Gemcitabine and platinum with duvelumab or pembrolizumab are the first line treatment option for advanced biliary tract cancers (BTC) patients.

• There is limited evidence for maintenance therapy in advanced BTC.

• Bevacizumab and erlotinib have individually and in combination shown efficacy advanced BTC.

• We report the Phase II results of a two-arm randomized multicentre integrated phase II-III trial to evaluate the efficacy of bevacizumab-erlotinib as ‘Switch’ maintenance after six months of gemcitabine-based chemotherapy

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INCLUSION CRITERIA & DESIGN

Inclusion criteria

18-75 years of age; Histologically confirmed advanced adenocarcinoma of the gallbladder cancer, intrahepatic cholangiocarcinoma, or perihilar cholangiocarcinoma

Received gemcitabine based chemotherapy for 6 months with at least stable disease on response evaluation (clinically and radiologically), ECOG PS 0-1 and adequate organ function.

Trial design and intervention

BEER- BTC is an integrated Phase II-Phase III randomised double arm multicentre study.

Enrolled Patients underwent permuted block randomization in a 1:1 ratio to bevacizumab-erlotinib arm (bevacizumab 5 mg/m² every 21 days along with an erlotinib 100 mg daily) or observation arm.

AIMS AND OBJECTIVES

• Primary endpoint: Progression-free survival (PFS), defined as the time from enrolment in the study until disease progression or death due to any cause.

• Secondary endpoint: Overall survival (OS), adverse events, proportion of treatment completion, and serious adverse events.

TUMOR & STATISTICAL ASSESSMENTS

Assessments

Tumor assessments were performed according to RECIST v1.1 every 2-3 months.

Adverse events were evaluated according to the CTCAE 5.0

Statistical analysis:

The baseline assumption was that patients on Observation arm will have a median PFS of 4 months. Assuming the bevacizumab-erlotinib combination increased PFS from four to eight months, with a power of 90% and alpha of 0.05, a Phase II randomized study required a total of 98 patients with study accrual period of 3 years (inclusive of an attrition rate of 10%).

PROGRESSION FREE SURVIVAL

CONCLUSIONS

• This multicenter investigator initiated study using bevacizumab-erlotinib as switch maintenance was well tolerated and achieved its primary endpoint of improving progression free survival compared to observation in patients with biliary tract cancers who had previously received six months of gemcitabine-based chemotherapy.

• The study now moves on to the phase III component of the trial evaluating improvement in overall survival as the primary outcome.

BASELINE CHARACTERISTICS

Characteristic Observation (n=48) Bevacizumab-erlotinib (n=48)

Age, years 52 (27-71) 49 (27-72)

Female gender 29 (59) 35 (71)

Gallbladder carcinoma 40 (82) 43 (87)

Cholangiocarcinoma 9 (18) 11 (22)

Metastatic 35 (71) 37 (76)

Locally advanced 14 (29) 12 (24)

Prior resection of primary tumor – no. (%) 13 (27) 16 (33)

Prior therapy

Semicitabine-cisplatin 45 (92) 42 (86)

Semicitabine - gemcitabine 0 2 (3)

Semicitabine- cisplatin - Nab Paclitaxel 4 (8) 5 (10)

CA 19.9 levels > upper limit of normal – n 14 (28) 20 (41)

Offered 2nd line chemotherapy 36 (73) 30 (61)

CONSORT DIAGRAM

DISCLOSURES AND CONTACT DETAILS

• The study received educational grants from Lupin Limited, and Intas Pharmaceuticals Limited. Bevacizumab was provided by Dr. Reddy’s Laboratories while erlotinib was provided to patients from study funds.

• drvikas.ostwal@gmail.com