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CLINICAL TRIAL/REAL WORLD DATA

PP059 Phase Ib and pharmacokinetics study of alpelisib and capecitabine in patients with advanced solid tumors

A.R. Lim[1], B.Y. Kim[2], J.H. Kim[1], M.H. Hyun[1], K.H. Park[1], Y.H. Kim[1], S.H. Lee*[1]

[1]Division of Medical Oncology, Department of Internal Medicine, Korea University Anam Hospital, Korea; [2]Korea University Cancer Research Institute, Korea University College of Medicine, Korea

Background: This phase Ib study was performed to demonstrate synergistic efficacy in combination capecitabine with alpleisib (phosphatidylinositol 3-kinase catalytic subunit p110α blockade) and determine the maximal tolerated dose (MTD) and recommended phase II dose (RP2D) of this combination regimen in patients with advanced solid tumors refractory to standard therapy. The safety profile, anti-tumor activity, and pharmacokinetics (PK) were conducted.

Methods: Dose escalation phases were conducted in patients with advanced colorectal cancers and breast cancers who were refractory to standard therapy regardless of PIK3CA mutation. Patients were administered orally once daily alpelisib (200mg and 300mg) and twice daily capecitabine (850mg, 1000mg, 1250mg orally, days 1—14) every 3 weeks. Standard "3+3" dose escalation was used to define the MTD. The effect of alpelisib on the PK of capecitabine was assessed.

Results: Patients with 7 colorectal cancer (2 PIK3CA mutation) and 6 breast cancer (6 PIK3CA mutation) were enrolled. The first three patients in dose level 0 (alpelisib 200mg twice daily, capecitabine 1000 mg/ m2 twice daily) had no dose-limiting toxicities (DLTs). In dose level 1 (alpelisib increased to 300 mg daily), one of six patients had DLT (grade (Gr) 3 hyperglycemia). When dose level 2 (alpelisib 300mg twice daily, capecitabine 1250 mg/m2 twice daily) was expanded to 4 patients, no patients had DLTs. The combination of alpelisib 300mg twice daily, and capecitabine 1000 mg/m2 twice daily was declared as the MTD/RP2D in patients with advanced solid tumors. The most common AEs were Gr 2-3 hyperglycemia (61.5%) and Gr 2 diarrhea (30.8%). Frequent all-grade, treatment-related AEs included Gr 2 oral mucositis (23.1%), Gr2 nausea (23.1%), Gr 2 fatigue (15.4%), and Gr 2 hand-foot syndrome (15.4%). Antitumor activity was observed in patients with PIK3CA mutant breast cancer (3 partial response and 3 stable disease in 6 patients). Alpelisib exposure (Cmax and AUC 0-12) was unaffected by concomitant capecitabine. There were no clinically relevant drug-drug interactions observed between alpelisib and capecitabine.

Conclusions: The combination of alpelisib and capecitabine is generally tolerated, without pharmacokinetic interactions, and shows antitumor activity in patients with PIK3CA mutant advanced cancers.

Keywords: *Alpelisib, PIK3CA, Phase Ib Study*

https://doi.org/10.1016/j.esmoop.2022.100731

PP060 Treatment patterns of chronic lymphocytic leukemia/small lymphocytic lymphoma in Korea: A multicenter retrospective study, KCSG LY20-06

J.S. Kim[1], T.M. Kim[2], M.J. Kang[3], S.A. Koh[4], H.K. Park[5], S-H. Nam[6], J.J. Han[7], G-W. Lee[8], Y.J. Yuh[9], H.J. Lee[10], J.H. Choi*[11]

[1]Department of Internal Medicine, Chungnam National University Sejong Hospital, Korea; [2]Department of Internal Medicine, Seoul National University Hospital, Korea; [3]Department of Internal Medicine, Inje University Haeundae Paik Hospital, Korea; [4]Department of Internal Medicine, Yeungnam University, Korea; [5]Department of Internal Medicine, Seoul National University Boramae Medical Center, Korea; [6]Department of Internal Medicine, VHS Medical Center; Kyung Hee University Hospital at Gangdong, Korea; [7]Department of Internal Medicine, Kyung Hee University, Korea; [8]Department of Internal Medicine, Gyeongsang National University Hospital, Korea; [9]Department of Internal Medicine, Inje University Sanggye Paik Hospital, Korea; [10]Department of Internal Medicine, Chosun University Hospital, Korea; [11]Department of Internal Medicine, Hanyang University Guri Hospital, Korea

Background: Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is the most common leukemia in Western countries. However, with a 20-fold lower incidence than the Western, real- world data in Korea is limited. Therefore, we aimed to evaluate recent changes in treatment patterns and survival outcomes of CLL/SLL in Korea.

Methods: We conducted a multicenter retrospective study in Korea. Patients diagnosed with CLL/SLL between January 2010 and March 2020 and who received chemotherapy were eligible.

Results: A total of 142 patients were included and were at the median age of 66 years at diagnosis (range, 38—95). Ninety-six (67.6%) patients were male, with the median interval from diagnosis to the initial treatment of 0.9 months (range, 0—77.6). The most common treatment indication was progressive marrow failure (50.0%). For the 1st-line treatment, 46.5% (66/142) received FCR (fludarabine, cyclophosphamide, and rituximab), followed by chlorambucil (19.7%) and GC (obinutuzumab and chlorambucil) (12.0%). After a median follow-up of 48.4 months, a median progression-free survival (PFS) was 46.4 months (95% confidence interval [CI], 31.7—61.4), and median overall survival (OS) was not reached (95% CI, 98.4 months—not reached). Patients treated with FCR demonstrated significantly increased median PFS than the non-FCR (31.7 vs. 61.4 months, $p = 0.0008$), but there was no significant difference in median OS (not reached for both, $p = 0.7684$). However, in patients aged over 65 years, there was no superiority in either median PFS (31.7 vs. 39.2 months, $p = 0.4522$) or median OS (74.1 vs. not reached, $p = 0.5114$). GC has been gained reimbursement in Korea from April 2017. Since then, GC has become the 2nd most common regimen (27.4%) after FCR (32.3%) overall and the most common (41.5%) among the population over 65 years of age. Chlorambucil was consistently chosen as the first-line agent during that period. For the 2nd line, ibrutinib was the most common regimen, comprising 80.0% after reimbursement in April 2018.

Conclusions: Age and reimbursement status were considered to have a significant influence in determining treatment strategy. Although treatment was inevitably affected by reimbursement status, survival outcomes were comparable to those in the West.

Keywords: *Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma, Reimbursement*

https://doi.org/10.1016/j.esmoop.2022.100732

PP065 Novel scoring system guiding the incorporation of adjuvant RT for incidental neuroendocrine neoplasms treated with surgical resection followed by chemotherapy

J. Kwon[1], B.H. Kim*[2]

[1]Department of Radiation Oncology, Chungnam National University School of Medicine, Korea; [2]Department of Radiation Oncology, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Korea

Background: This study aimed to investigate the role of adjuvant radiotherapy (RT) in incidentally found neuroendocrine neoplasms treated with primary resection and systemic chemotherapy and help clinicians decide on the incorporation of adjuvant RT based on individualized prediction.

Methods: We searched the Surveillance, Epidemiology, and End Results database and identified 294,810 patients with neuroendocrine carcinoma. We selected 4,324 patients who met the inclusion/exclusion criteria for the following analyses. As the patients treated with RT were not assigned randomly, we used propensity score matching (PSM).

Results: Three-year overall survival was 54.2% in the cohort, and the median follow-up was 24 months. The most common histology was small cell carcinoma (SCC), followed by neuroendocrine carcinoma and carcinoid tumor. All patients received chemotherapy. However, RT was administered to 1693 (39.2%) patients only. RT group had more unfavorable features, including higher proportion of SCC (56.8% vs. 38.4%), N2/3 stage (21.2% vs. 10.5%), and poorly/undifferentiated tumors (86.2% vs. 74.1%). After PSM, old age, male sex, SCC, advanced T or N stage, poorly/undifferentiated tumors, large primary tumor size, and no use of RT were all significantly associated with a poor prognosis. After multivariate analysis, the survival benefit of RT was also preserved (HR 0.82, 95% CI 0.73−0.91, $p < 0.001$). Subgroup analysis suggested that primary site (thorax or GU/GY), poorly differentiated tumors, SCC, small tumor size (< 2cm), or LN negativity were the factors for which adjuvant RT appeared desirable. To help clinical decisions for RT, we proposed a novel scoring system based on the factors mentioned above (site-thorax or GU/GY, poorly differentiated tumor, tumor size <2cm, LN negativity). When examining the benefit of adjuvant RT based on individually calculated scores, we found that RT significantly increased survival in patients with scores of 2—4 but not in patients with scores of 0—1.

Conclusions: Our study highlights the necessity of guiding adjuvant RT in incidentally found neuroendocrine neoplasms. However, because the benefits depend on various clinicopathologic characteristics, RT should be recommended in carefully selected patients. We proposed a novel scoring system that could predict survival benefit obtained from RT for these rare types of cancer.

Keywords: *Neuroendocrine Carcinoma, Radiotherapy, Surgery*

https://doi.org/10.1016/j.esmoop.2022.100733