MYELOPROTECTION WITH TRILACICLIB REGARDLESS OF RISK OF CHEMOTHERAPY-INDUCED FEBRILE NEUTROPENIA AND/OR ANEMIA/RED BLOOD CELL TRANSFUSIONS

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INTRODUCTION

• Chemotherapy-induced myelosuppression (CIM) is one of the most common dose-limiting complications of chemotherapy, and is associated with a range of debilitating complications, which can have a significant impact on patient care8

• Febrile neutropenia (FN) and anemia are two clinically important manifestations of CIM that can negatively impact patient outcomes, and often incur significant costs9

• Trilaciclib is a transmembranous CKD4 inhibitor administered prior to chemotherapy to reduce the occurrence of CIM8

• Trilaciclib transiently arrests hematopoietic stem and progenitor cells in the G1 phase of the cell cycle during chemotherapy exposure to preserve bone marrow and immune system function from chemotherapy-induced damage (myelopreservation)9

• The myelopreservation benefits of trilaciclib have been shown in three randomized, double-blind, phase 2 studies in patients with extensive stage small cell lung cancer (SCLC)7

• Consistent with findings from the initial studies, a pooled analysis of these data showed that administering trilaciclib prior to chemotherapy resulted in less hematologic toxicity, reduced the use of supportive care interventions, and improved quality of life7

• Using the pooled dataset, the aim of this analysis was to examine if patients at varying risk for FN or anemia/red blood cell (RBC) transfusions derived the same benefits from trilaciclib

METHODS

• Data were pooled from patients enrolled in the studies outlined in Table 1 (intention-to-treat population)

• Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) and use of erythropoiesis-stimulating agents (ESA) was prohibited in cycle 1, although therapeutic G-CSF was allowed after cycle 1, supportive care, including G-CSF and ESAs, was allowed as needed. RBC and platelet transfusions were allowed per investigator discretion throughout the entire treatment period

TABLE 1. OVERVIEW OF TRILACICLIB CLINICAL STUDIES INCLUDED IN POOLED ANALYSIS

| Study | Patient Population | Treatment Schedule | Study Design | Chemotherapy Regimen | Baseline Risk Factors
|-------|---------------------|--------------------|-------------|---------------------|---------------------|
| G1282-D | Non-small cell lung cancer (NSCLC) | Trilaciclib 40 mg/m² IV QD or placebo IV QD prior to chemotherapy on days 1-3 of each 21-day E/P cycle | Phase 2 study | Etoposide/carboplatin | Age, performance status, clinical comorbidities, prior chemotherapy?
| G1282-JS | Non-small cell lung cancer (NSCLC) | Newly diagnosed Stage IIIB/IV | Phase 3 study | Etoposide/cisplatin | Age, performance status, clinical comorbidities, prior chemotherapy?
| G1282-JS | Previously treated Stage IIIB/IV | Trilaciclib 40 mg/m² IV QD or placebo IV QD prior to platinum 1.5 mg/m² IV QD on days 1-5 of each 21-day cycle | Phase 2 study | Etoposide/cisplatin | Age, performance status, clinical comorbidities, prior chemotherapy?

1FEMA temporarily suspended all other trilaciclib trials; 2Adapted from: Coiffier B, et al. Clin Cancer Res. 2019;25:18-26. 2BPM; 3BPM not met during the study period; 4BPM not met prior to study initiation; 5BPM not met at study start; 6premedication with oral dexamethasone 10 mg in each of 3 days between days 1 and 21 (4 mg for cycle 1 only); 7premedication with oral dexamethasone 10 mg in each of 3 days between days 1 and 21 (4 mg for cycle 1 only); 8premedication with oral dexamethasone 10 mg in each of 3 days between days 1 and 21 (4 mg for cycle 1 only); 9premedication with oral dexamethasone 10 mg in each of 3 days between days 1 and 21 (4 mg for cycle 1 only)

• Six baseline factors associated with an increased risk of FN and four baseline factors associated with an increased risk of anemia (ESAs) were used to classify patients into four FN risk categories (1, 2, 3, and 6-5 risk factors) and three anemia risk categories (1, 2, and 3-4 risk factors)

TABLE 2. BASELINE FACTORS ASSOCIATED WITH AN INCREASED RISK OF FEBRILE NEUTROPENIA AND/OR ANEMIA/RED BLOOD CELL TRANSFUSIONS

<table>
<thead>
<tr>
<th>Baseline Risk Factors</th>
<th>FN Risk Category</th>
<th>Anemia Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Performance status</td>
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<td>Yes</td>
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<tr>
<td>Clinical comorbidities</td>
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<td>Yes</td>
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<tr>
<td>Prior chemotherapy</td>
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<td>Yes</td>
</tr>
<tr>
<td>Baseline hematopoiesis</td>
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<td>Yes</td>
</tr>
<tr>
<td>EOCF PS</td>
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<td>Yes</td>
</tr>
<tr>
<td>Prior cytopoiesiotherapy</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

CIM: chemotherapy-induced myelosuppression; EOCF: PL; P.E.: Cooperative Group performance status; RBC: red blood cell

Subgroup analyses were conducted to evaluate the impact on:

• Neutropenia-related endpoints: mean duration of severe (grade 4) absolute neutrophil count <0.5 x 10⁹ cells/L neutropenia (DSN) in cycle 1 and the percentage of patients with severe neutropenia (SN)

• RBC-related endpoints: percentage of patients with grade 3-4 decreased hemoglobin levels (anemia) and RBC transfusions on/wk 5

RESULTS

• Six baseline factors associated with an increased risk of FN and four baseline factors associated with an increased risk of anemia (ESAs) were used to classify patients into four FN risk categories (1, 2, 3, and 6-5 risk factors) and three anemia risk categories (1, 2, and 3-4 risk factors)

Patient disposition and baseline characteristics

• The pooled efficacy analysis comprised 123 and 119 patients who received trilaciclib or placebo prior to chemotherapy, respectively

• As described previously, patient demographics and baseline disease characteristics were generally comparable between treatment groups

• Patient distribution across the FN and anemia risk categories (Table 3) was comparable between the treatment groups

Subgroup analysis for red blood cell-related endpoints by anemia risk factors

• Effects on RBC-related endpoints (occurrence of grade 3-4 decreased hemoglobin levels and RBC transfusions on/off week 5) consistently favored trilaciclib versus placebo across the anemia risk factors and categories, including those at the highest risk of anemia/RBC transfusions (Table 5; Figures 3 and 4)

CONCLUSIONS

• Compared with placebo, the myelopreservation benefits of trilaciclib were observed regardless of the underlying risk for FN or anemia/RBC transfusions, indicating that trilaciclib is effective at reducing CIM regardless of risk category, including in patients with the highest risk