Jazz Pharmaceuticals

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Request for review of clinical data on lurbinectedin by the NCCN Panel for Small Cell Lung Cancer (SCLC)

On behalf of Jazz Pharmaceuticals, I respectfully present the clinical data[1] for lurbinectedin for review by the NCCN SCLC Panel. The PDUFA date for lurbinectedin is August 16, 2020.

Specific Changes: Please consider adding lurbinectedin when it receives approval:

SCL-E 2 of 4: SCLC Subsequent Systemic Therapy

- "Relapse ≤6 months": Lurbinectedin under "Preferred Regimen"
- "Relapse >6 months": Lurbinectedin as Preferred Regimen

FDA Clearance: Lurbinectedin is currently under Priority Review, seeking accelerated approval by the FDA for the treatment of patients with SCLC who have progressed after prior platinum-containing therapy. Jazz will notify NCCN when lurbinectedin is approved.

Rationale: Relapsed SCLC remains a significant unmet need as prognosis is poor after failure of initial therapy.[2] In SCLC patients treated with lurbinectedin after initial platinum-based chemotherapy with or without immunotherapy, clinical responses were observed both in patients who were chemo-sensitive and chemo-resistant, without the use of granulocyte colony-stimulating factors (G-CSF) as primary prophylaxis.[1]

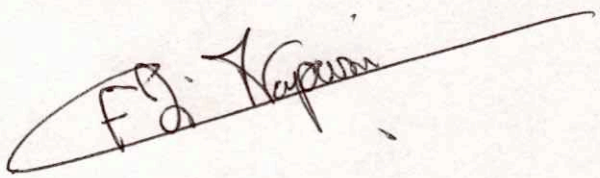
Supporting Literature: The registrational phase 2 study included 105 patients with SCLC pretreated with one prior chemotherapy-containing line, including patients with prior exposure to immunotherapy.[1] Extensive stage disease at diagnosis was evident in 73 (69.5%) patients. Treatment consisted of lurbinectedin 3.2 mg/m^2 administered as a 1-hour intravenous infusion every 3 weeks. At a median follow-up of 17.1 months, overall response rate, (ORR), the primary

endpoint of the trial was 35.2%. Responses were observed in both chemo-sensitive (ORR 45.0%) and chemo-resistant (ORR 22.2%) cases.[1] Chemo-resistant disease was defined as chemotherapy-free interval (CTFI) less than 90 days, including 20% of patients of very poor prognosis with CTFI less than 30 days. Median duration of response was 5.3 months. Median progression-free survival and overall survival in the overall population was 3.5 months and 9.3 months, respectively. Among SCLC patients who had an initial objective response, median OS was 12.6 months in the overall population, 15.8 months in the chemo-sensitive group, and 10.9 months in the chemo-resistant group.[1]

In an exploratory analysis of patients with CTFI greater than 6 months (n=20), ORR was 60%, and median OS was 16.2 months.[3] (*Important Note: These data in the preceding sentence are subject to embargo. As such, they are not in the public domain and are expected to be treated as confidential by NCCN and its members and may not be discussed or disclosed outside of this review panel. Jazz will notify NCCN when the data are in the public domain.)*

The most common adverse events in the study were neutropenia (71.4%; grade 3/4, 45.7%); febrile neutropenia (4.8%), fatigue (58.1%; grade 3, 6.7%), decreased appetite (21.0%), nausea (32.4%) and vomiting (18.1%).[1] Primary prophylactic G-CSF was not allowed, and 21.9% patients received G-CSF as secondary prophylaxis or therapeutic treatment for neutropenia. Serious treatment-related adverse events occurred in 10.5% of patients. Two patients (1.9%) discontinued lurbinectedin due to treatment-related adverse events. No treatment-related deaths were reported.[1]

Sincerely,



References:

1. Trigo J, et al. Lurbinectedin as Second-line Treatment for Small Cell Lung Cancer Patients: Results from a Single-arm Phase 2 Study. *Lancet Oncology*. 2020. [Epub ahead of print] (**enclosed**)
2. NCCN Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer. V3.2020.
3. Subbiah V, et al. Activity of Lurbinectedin in Second-line SCLC Patients Who Are Candidates for Platinum Re-challenge. **Data on file, subject to embargo.**