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NCCN Guidelines Panel: B-Cell Lymphomas

On behalf of Verastem, Inc. (Verastem), I respectfully request the NCCN B-Cell Lymphomas Guideline Panel to consider the enclosed data for duvelisib for the treatment of patients with relapsed/refractory follicular lymphoma (R/R FL).

Specific Changes: Please consider the following:
  - FOLL-B 2 of 4:
    - Add duvelisib under “Second-line and Subsequent Therapy”

FDA Clearance: On September 24, 2018, the FDA approved duvelisib for the treatment of adult patients with:
  - Relapsed or refractory CLL or SLL after at least two prior therapies
  - Relapsed or refractory follicular lymphoma after at least two prior systemic therapies

Rationale:
Duvelisib, an oral inhibitor of PI3K-δ (delta) and PI3K-γ (gamma), demonstrates significant clinical activity as monotherapy in patients with R/R FL as demonstrated by median progression-free survival (mPFS), overall response rate (ORR), and overall survival (OS).

Supporting Literature: Flinn et al. reported results of a Phase 2, open-label, single arm DYNAMO study of duvelisib in patients with refractory FL (n=83) (1,2). Patients on the study were double refractory, i.e. lack of CR or PR; or PD within 6 months of a qualifying regimen of both rituximab (monotherapy or in combination) and to chemotherapy or radioimmunotherapy. The primary endpoint of the study was ORR, with overall response defined as complete response (CR) or partial response (PR). Secondary endpoints included duration of response (DOR), PFS, and OS. Patients had a median of 3 prior lines of therapy (range: 1 to 10), with 94% being refractory to their last therapy and 81% being refractory to 2 or more prior lines of therapy. After a median follow-up time of 11.5 months, ORR per blinded Independent Review Committee (IRC) was 41% (all PR). Per IRC, median PFS and DOR was 8.3 months and 7.9 months, respectively. Median OS was 27.8 months. The safety profile of duvelisib was considered manageable. Most common grade 3 adverse events (greater than or equal to 5%) included diarrhea (16%), anemia (11%), febrile neutropenia (8%), neutropenia (7%), thrombocytopenia (7%), fatigue (7%), vomiting (7%), and rash (5%). Most common grade
4 adverse events (greater than or equal to 5%) were neutropenia (15%) and lipase increase (6%). 

In summary, duvelisib demonstrated a manageable safety profile and significant clinical activity in refractory FL.

The following key study publications are submitted, including the FDA prescribing information.


Sincerely,

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