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NCCN Guidelines Panel: Hairy Cell Leukemia (HCL)

Dear Sir or Madam:

On behalf of Innate Pharma, this letter is a request to the NCCN Hairy Cell Leukemia Panel regarding updating LUMOXITI® (moxetumomab pasudotox-tdfk) to category 1 for the treatment of adult patients with relapsed or refractory (R/R) HCL based on long-term follow-up results from the phase 3 pivotal trial 1053.[1]

Specific Changes on NCCN Guideline page HCL-2:
We respectfully request moxetumomab pasudotox to be updated to category 1 for R/R HCL based on long-term (median follow-up 24.6 months) final analysis of the pivotal phase 3 study.

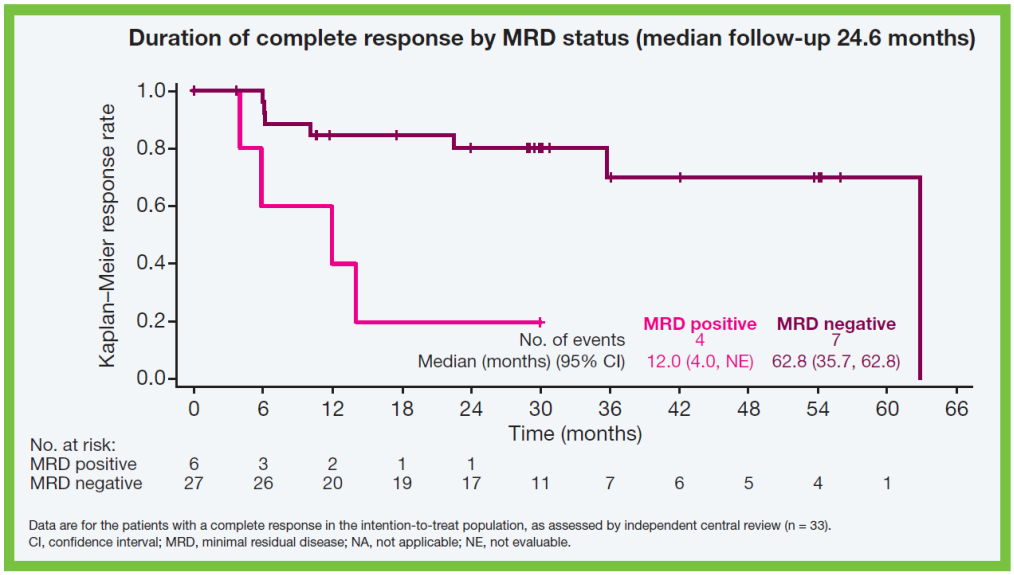
- Study 1053 is the largest phase 3 prospective study to date in the R/R setting for this rare disease.[1] It was conducted at 32 centers in 14 countries and included 80 patients. Efficacy responses were assessed by a blinded independent central review.
- High rate of deep and durable responses: 36.3% durable CR (CR with HR > 180 days) and 32.5% CR with HR ≥ 1 year[1]
- Moxetumomab pasudotox is the first new FDA-approved treatment option for R/R HCL in over 20 years.[2]

FDA Clearance:[2]
Moxetumomab pasudotox-tdfk was approved by the FDA for the treatment of adult patients with R/R HCL who received at least two prior systemic therapies, including treatment with a purine nucleoside analog. Not recommended in patients with severe renal impairment (CrCl ≤ 29 mL/min).[1] Please refer to the prescribing information for details (enclosed).

Study 1053 Update:[1]
Study 1053 is the pivotal, phase 3, single-arm, open-label study of moxetumomab pasudotox conducted at 32 centers in 14 countries. This is the largest prospective study in third line or beyond R/R HCL (n=80). A blinded independent central review assessed efficacy responses. The median number of prior systemic therapies received was 3.0; 48.8% of patients were refractory to purine nucleoside analogs (PNA) and 37.5% were unfit for PNA re-treatment. The primary efficacy endpoint in Study 1053 is durable complete response (CR).
Final long-term results of study 1053 at a median follow-up of 24.6 months.

Durable CR	36.3%
MRD-negativity among durable CR	89.7%
Duration of HR from onset of CR	62.8 months
Durable CR with HR ≥1 y	32.5%
CR	41.3%
MRD negativity among CR	81.8%
Median duration of CR	62.8 months
ORR	75%
Median PFS	41.5 months

HR: hematologic remission; MRD: minimal residual disease.



Moxetumomab pasudotox-tdfk displayed a manageable safety profile. The most common treatment-related adverse events (TRAE) were nausea (28%), peripheral edema (26%), headache (21%), and pyrexia (20%). Serious AEs were reported in 35% of patients, the most common being hemolytic uremic syndrome (HUS, 7.5%), pyrexia (6.3%), and capillary leak syndrome (CLS, 5.0%). CLS and HUS that occurred were generally manageable and reversible. TRAE led to discontinuation in 10% patients. This follow-up analysis showed no decline in renal function over time, suggesting that current strategies for monitoring and managing CLS and HUS are effective. Two deaths occurred due to an adverse event (pneumonia and septic shock) which were considered unrelated with the study treatment; another two deaths occurred due to disease progression.

Sincerely,

Ronak Savla

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References (**enclosed**):

1. Kreitman RJ, Dearden C, Zinzani PL, et al. Moxetumomab pasudotox-tdfk in heavily pretreated patients with relapsed/refractory hairy cell leukemia: long-term follow-up from the pivotal phase 3 trial. Presented at the 61st American Society of Hematology Annual Meeting and Exposition, December 7–10, 2019, Orlando, FL, USA. **[Manuscript submitted**].
2. LUMOXITI® (moxetumomab pasudotox-tdfk) Prescribing Information.