MultipleMyelomaHub

Relapsed/refractory patients

EMA CHMP recommends elotuzumab in combination with pomalidomide and dexamethasone for relapsed/refractory multiple myeloma

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The European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion, recommending the approval of elotuzumab (E) in combination with pomalidomide (P) and low-dose dexamethasone (d, EPd) for patients with relapsed/refractory multiple myeloma (RRMM).[1,2]

The recommendation is for the treatment of patients who have received ≥ two prior lines of therapy, including lenalidomide and a proteasome inhibitor (PI), and who progressed with their last therapy.[1] This is based on the ELOQUENT-3 study, which showed EPd reduced the risk of progression or death by 46% compared with Pd in patients with RRMM.[3]

Elotuzumab was originally approved by the EMA in combination with lenalidomide and dexamethasone for patients with RRMM who received at least one prior line of therapy.[4] The United States (US) Food & Drug Administration (FDA) have already approved the EPd triplet in patients with RRMM in November 2018.[5]

Background[2]

Elotuzumab specifically targets the signaling lymphocyte activation molecule family member 7 (SLAMF7) which is a cell surface glycoprotein expressed on MM cells as well as natural killer (NK) cells, plasma cells, and in low-levels on other hematopoietic cells. Therefore, elotuzumab has a dual mechanism of action:

1. Activates the immune system via NK cells by the SLAMF7 pathway
2. Direct targeting of SLAMF7 on MM cells, tagging them for NK-cell-mediated destruction by antibody-dependent cellular toxicity

Elotuzumab is administered as an intravenous (IV) injection.

ELOQUENT-3 trial[2,3,6]

ELOQUENT-3 (NCT02654132) is a randomized, open-label, phase II trial, of EPd *versus* Pd in patients with RRMM. The results of the ELOQUENT-3 trial were presented by Professor Meletios A. Dimopoulos at the European Hematology Association (EHA) congress in June 2018.[3]

Data given as EPd versus Pd unless otherwise stated

- Patients (N= 117) were randomized to either EPd (n= 60) or Pd (n= 57)

- IV E: 10mg/kg weekly for the first two 28-day cycles, then 20mg/kg every four weeks
- Oral P: 4mg daily on days 1–21 of each 28-day cycle
- d: 40mg weekly
    - Reduced to 20mg for patients >75 years old
- Administered until disease progression (PD) or unacceptable toxicity
- Primary endpoint: investigator-assessed progression-free survival (PFS)
- Secondary endpoints: overall response rate (ORR) and overall survival (OS)
- Median age: 67 years
- Median prior lines of treatment: 3 (2–8)
- 87% of patients were refractory to lenalidomide, 80% to a PI, and 70% to both
- At the time of datacut (21st February 2018), with a minimum follow up of 9.1 months, 40% (24/60) patients remained on EPd and 20% (11/55) on Pd
- Main reason for discontinuation was PD (EPd 43% *vs* Pd 56%)

In the trial, EPd doubled the median PFS and ORR compared to Pd (**Table 1**). Whilst survival data was not mature, there was a positive trend for EPd compared to Pd. Safety data showed the EPd regimen was well-tolerated (**Table 2**) and a low rate of infusion-related reactions in the EPd arm (3.3%).

Table 1. Efficacy data from ELOQUENT-3 trial[2,6]

	EPd (n=60)	Pd (n=57)	Statistics	*p* value
Median PFS*	10.25 months 95% CI 5.59–not estimable (NE)	4.67 months 95% CI 2.83–7.16	Hazard ratio (HR) 0.54 95% CI 0.34–0.86	0.0078

ORR	53.3% 95% CI 40.0–66.3	26.3% 95% CI 15.5–39.7	Odds ratio (OR) 3.25 95% CI 1.49–7.11	0.0029

* Minimum follow-up of 9.1 months

Table 2. Safety data from the ELOQUENT-3 trial[2,6]

	EPd (n=60)	Pd (n=55)
Serious adverse events (SAEs)	22%	15%
Most common SAEs		
Pneumonia	13%	11%
Respiratory tract infection	7%	3.6%
AEs*		
Constipation	22%	11%
Hyperglycemia	20%	15%
Pneumonia	18%	13%
Diarrhea	18%	9%

Respiratory tract infection	17%	9%
Bone pain	15%	9%
Dyspnea	15%	7%
Muscle spasms	13%	5%
Peripheral edema	13%	7%
Lymphopenia	10%	1.8%

* with a ≥10% incidence in EPd arm, and ≥5% incidence in Pd arm

References

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