Selinexor in combination with Daratumumab-Bortezomib and dexamethasone for the treatment of relapse or refractory Multiple Myeloma: updated results of the phase 2, multicenter GEM-SELIBORDARA study

Submitted to Haematologica

Abstract ASH21, EHA23 y SEHH23

METHODS

Key inclusion criteria:

- **PART 1**: ≥ 3 PL, prior exposure to proteasome inhibitor (PI) and immunomodulatory drugs and refractory to the last line or double refractory.
- **PART 2**: relapse or progressive disease after ≥ 1 PL.

Study overview and treatment schedule:

PART 1

Daratumumab (16mg/kg IV/SC) weekly C1 and C2, C3-C6 Q2W, C7+ Q4W
Bortezomib (1.3 mg/m2 sc): d 1, 8, 15 & 22 (C1-C8), d1 & 15 (C9+).
Dexamethasone 40 mg d1, 8, 15 & 22
Selinexor 100 mg d1, 8, 15 & 22

4-week duration cycles

PART 2

Daratumumab (16mg/kg IV/SC) weekly C1 and C2, C3-C6 Q2W, C7+ Q4W
Bortezomib (1.3 mg/m2 sc): d 1, 8, 15 & 22 (C1-C8), d1 & 15 (C9+).
Dexamethasone 40 mg d1, 8, 15 & 22
Selinexor 60 mg d1, 8, 15 & 22

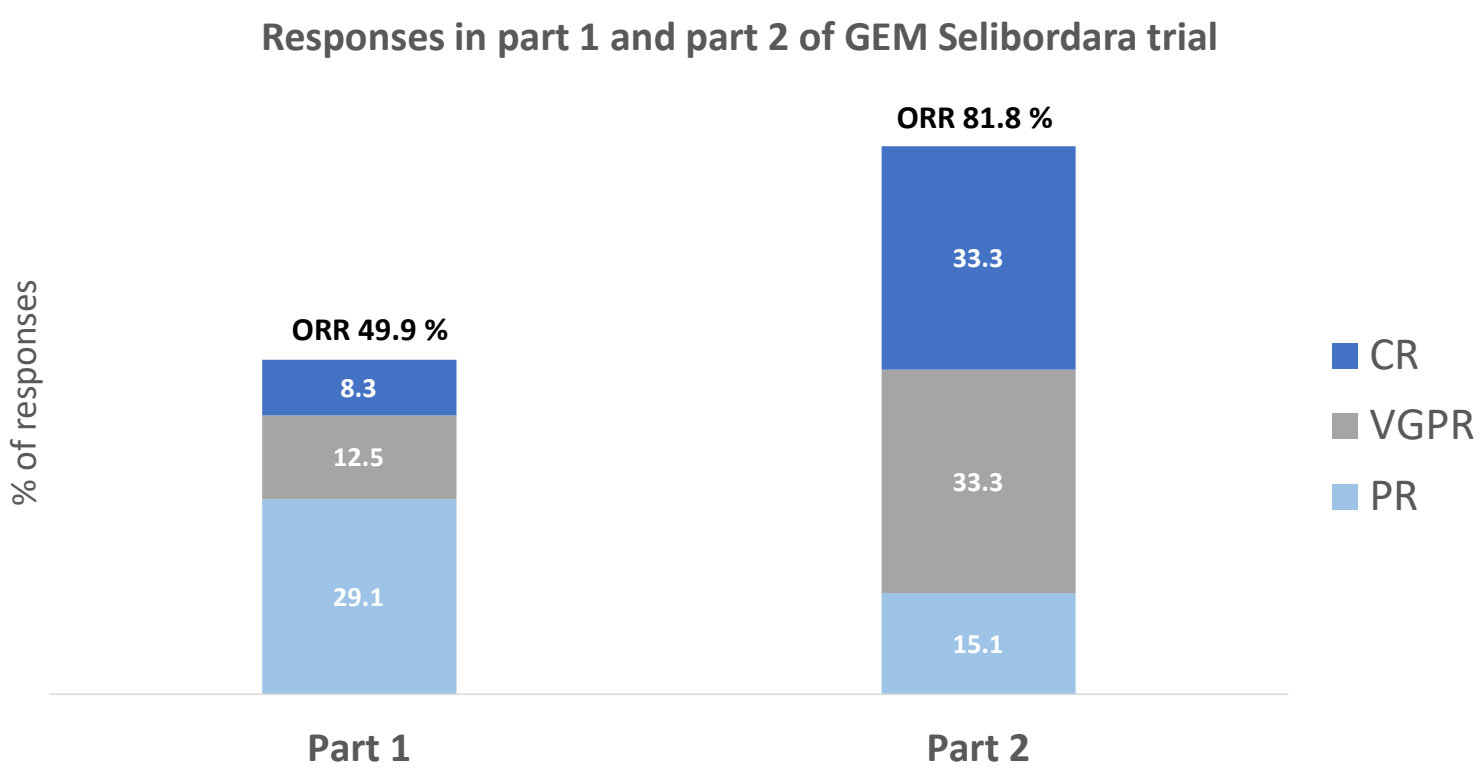
5-week duration cycles

Treatment was continued until disease progression or unacceptable toxicity.

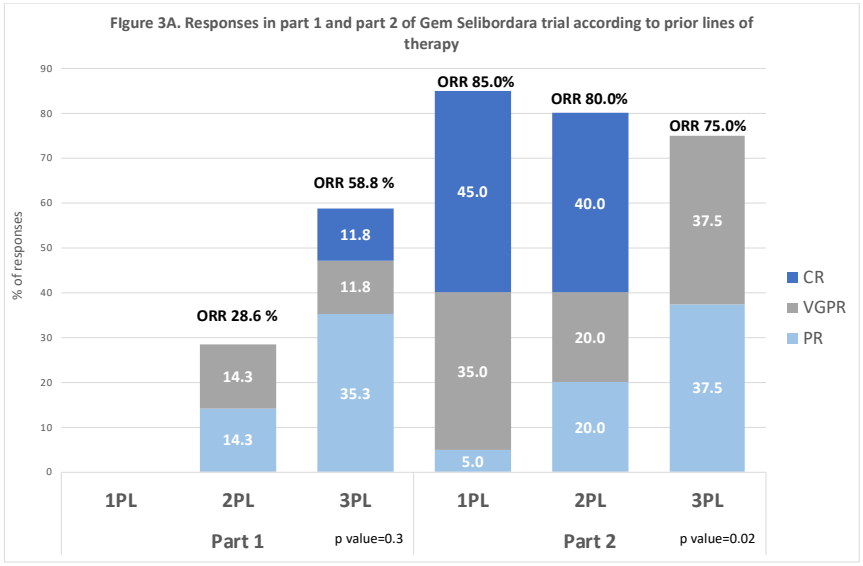
- Primary endpoint: complete response (CR) rate.
- Key secondary endpoints: ORR and safety profile.

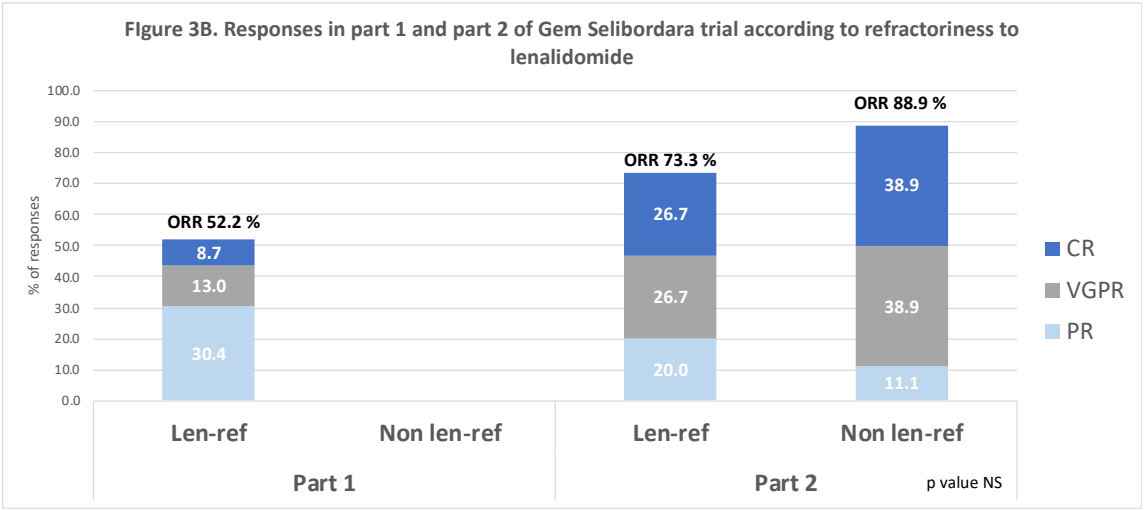
Study was conducted following Declaration of Helsinki and ICHGCP guidelines.

Responses achieved in the ITT Population with S-DVd in part 1 and part 2 of GEM Selibordara trial

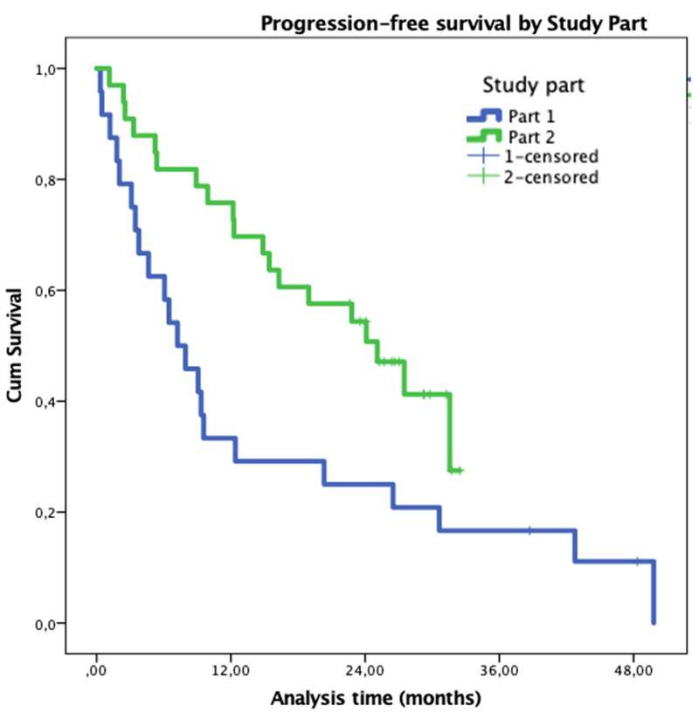


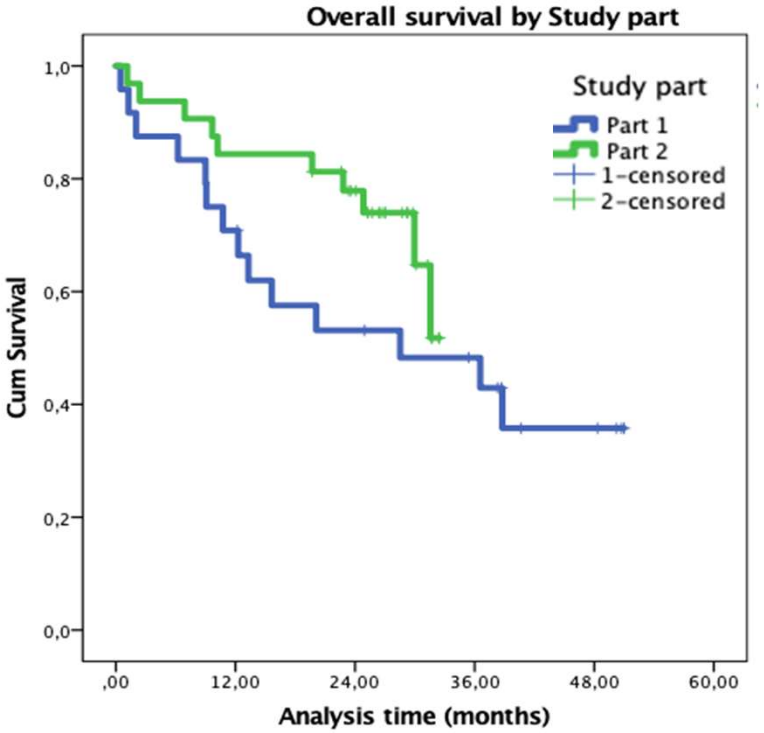
Responses achieved in the ITT Population with S-DVd in part 1 and part 2 of GEM Selibordara trial by number of prior lines of treatment (3A) and refractoriness to lenalidomide (3B)





Progression-free survival for the ITT Population in part 1 and part 2



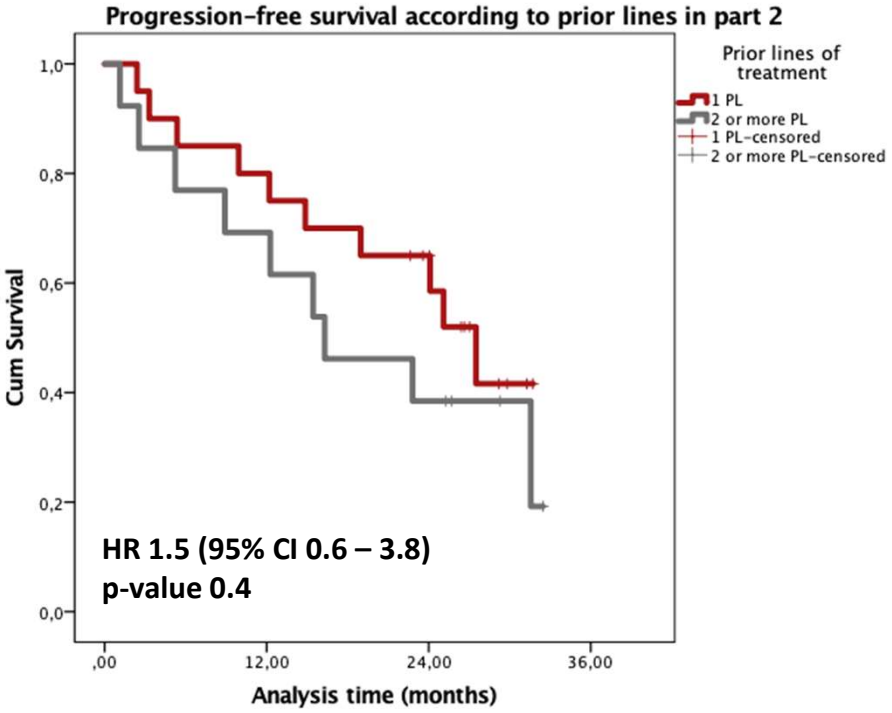


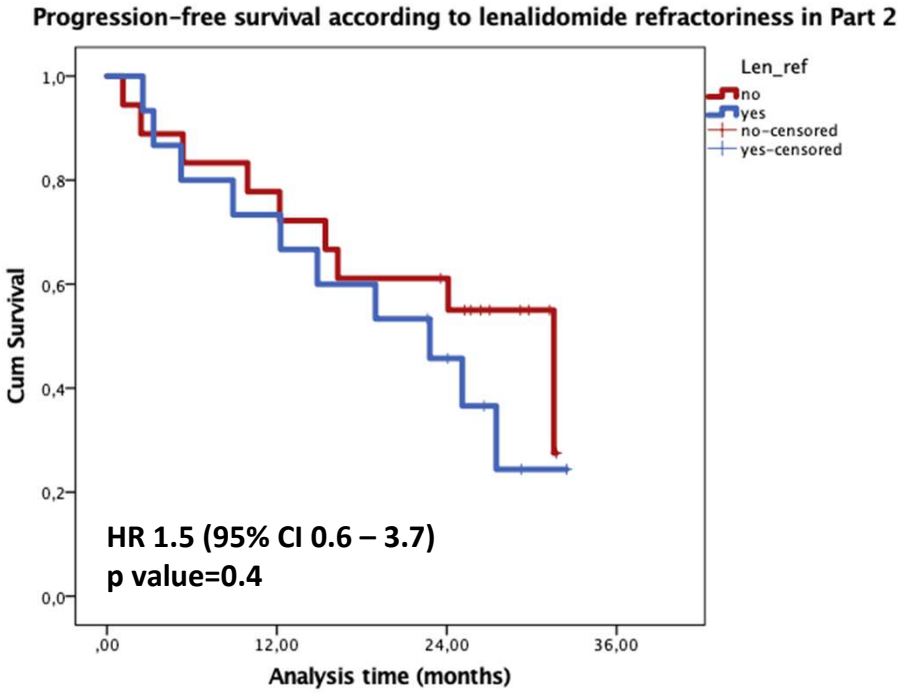
Parte 1 Con mediana de seguimiento de 40 meses (12-51), la mediana de **SLP fue de 7,2 meses** (95% CI 3,6 – 10,8) y la mediana de SG fue de 28,5 meses (IC del 95%: 0 a 57,9. (Figura 3A y 3B)

En la **parte 2** (n=33). Después de una mediana de seguimiento de 26 meses (19-31), la **mediana de SLP fue de 25,1 meses** (95% CI 16,0 – 34,2). En los **ref-len fue de 22,8 meses** (95% CI 11,6 – 34,0) y de 27,5 meses para los que recayeron tras 1LP

La mediana de SG no alcanzada.

Progression-free survival for the ITT Population in part 1 and part 2





Seguridad

Los eventos adversos (EA), más frecuentes fueron hematológicos [trombocitopenia (70,2%; grado 3-4: 65%) y neutropenia (38,6%; G3-4: 77%)], seguido de infecciones (74%) y toxicidad gastrointestinal [diarrea (38,6%) y náuseas (35,1%)].

No hubo diferencias significativas entre la parte 1 y 2 del estudio.

La dosis de selinexor fue la modificada con mayor frecuencia (10 casos en la parte 1 y 20 en la parte 2) y suspendida en 8 pacientes (5 de la parte 1 y 3 de la parte 2).

Un paciente salió del ensayo debido a toxicidad relacionada con el tratamiento.

CONCLUSIONES

Although cross-trial comparisons have important limitations, we postulate than adding selinexor to DVd, resulted in deep and durable responses, with apparently longer PFS as compared to DVd based on CASTOR results, especially in len-refractory patients.

Moreover, the addition of daratumumab to SVd appears also to clearly improve the results obtained with SVd in the BOSTON trial.

In conclusion, S-DVd might be an attractive option for len-refractory but daratumumab-sensitive patients if cardiovascular comorbidities are a concern or oral formulations are preferred.