

USE OF DARATUMUMAB BASED TREATMENTS IN PATIENTS WITH MULTIPLE MYELOMA AND HEPATIC IMPAIRMENT

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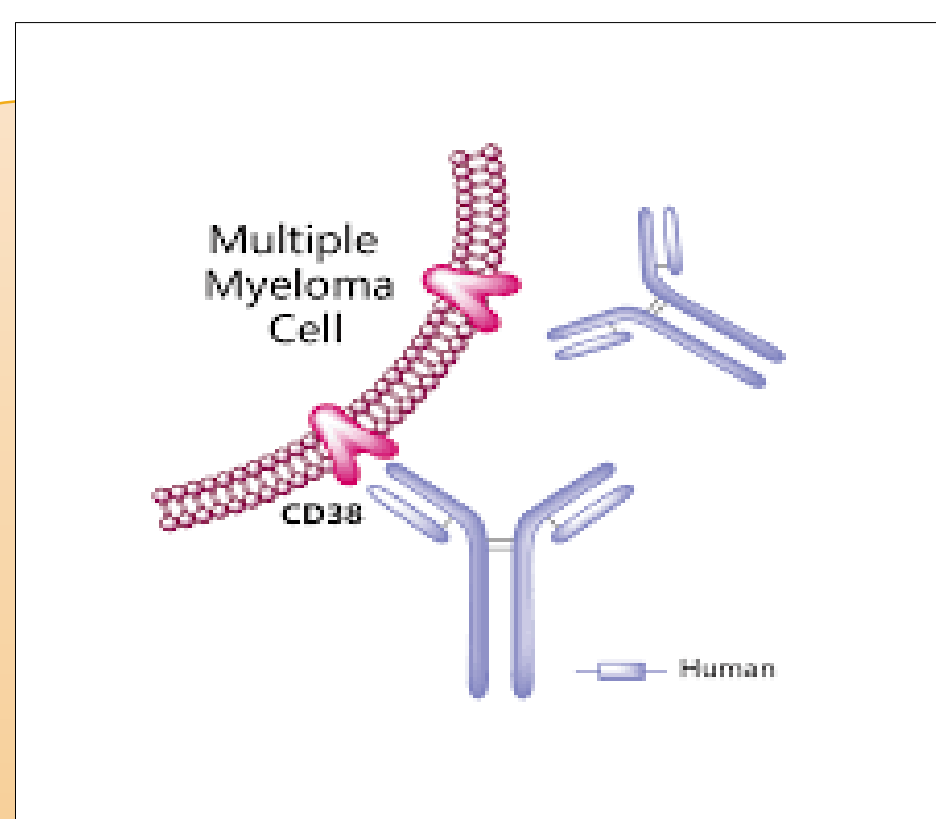
L01 - Cytostatics

BACKGROUND

✓ There is literature –**subgroup analysis**- suggesting lack of benefit for **daratumumab drug combinations** in patients with **untreated multiple myeloma (MM)** and **hepatic impairment (HI)**.

AIM

To conduct a systematic search and **methodological interpretation** of **subset analysis** about the use of **daratumumab-based treatments** in patients with **untreated MM** and **HI**.



Bibliographic review in Pubmed® (October 11, 2020)

MATERIAL AND METHODS

✓ Review strategy in “Clinical Queries/Narrow” tool: **(Therapy/Narrow[filter]) AND (daratumumab AND myeloma)**

✓ Inclusion criteria: Randomized clinical trials (**RCTs**) with **subset analyzes** according to baseline **hepatic function** for **overall survival (OS)** or **progression-free survival (PFS)**

✓ Two **methodologies**

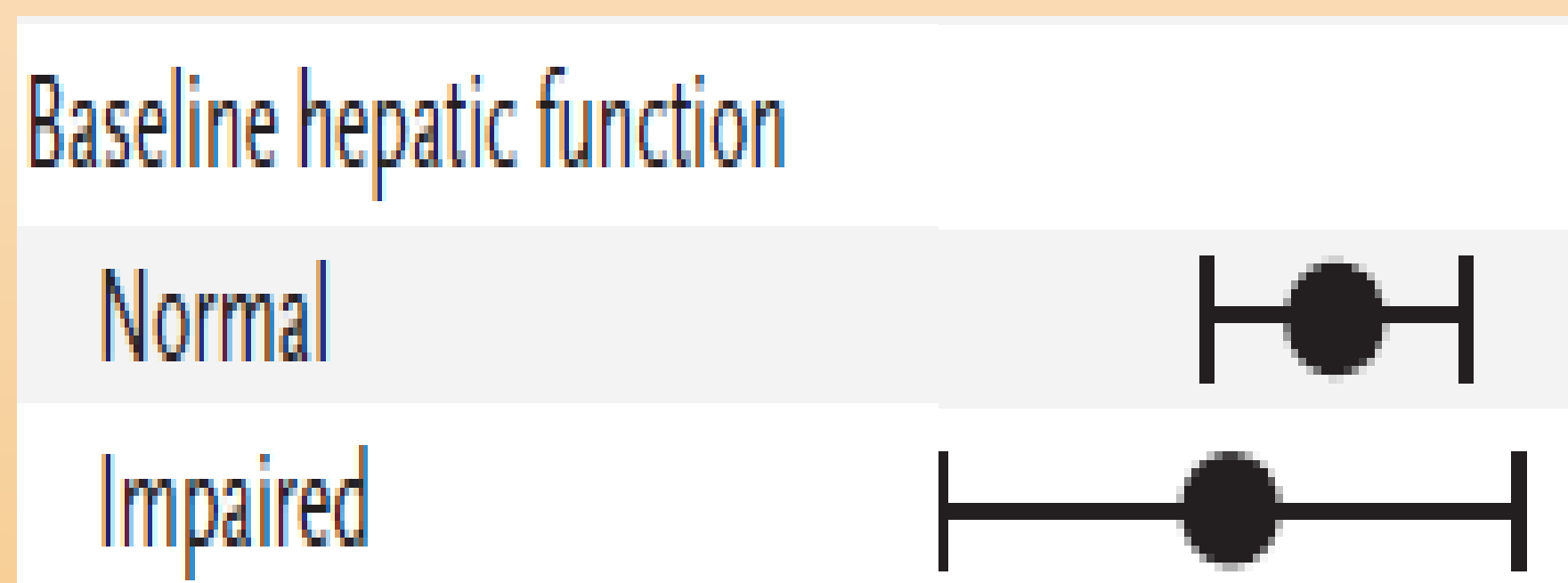
1^o Consideration of heterogeneity of subgroups ($p < 0.1$), prespecification, biological support and consistency

2^o Validated tool with preliminary questions to discard subgroup analyzes without minimal relevance and checklist → Recommendations of applicability

RESULTS

Results of bibliographic review:

25 results



22 results excluded

3 RCTs included

- ✓ 10 without design of RCT
- ✓ 9 studies with different clinical context
- ✓ 2 evaluated different drugs
- ✓ 1 without subset analysis



1^o Methodology

- Heterogeneity of subgroups: statistical interaction among subsets was observed for **PFS** in **1 RCT**.
- Pre-specification: subgroups pre-specified in each endpoint of **all RCTs**
- Biological support: It was reasoned in **all RCTs**.
- Consistency: No consistency of these subset analysis was found



2^o Methodology (validated tool)

Preliminary questions discarded applicability of subset analysis in 2 RCTs.

Recommendation in the remaining RCT: checklist recommended a “**null**” application of subgroup analysis for **PFS** because of inconsistency of results

CONCLUSION

No differences in **OS** or **PFS** according to **baseline hepatic function** should be considered for **daratumumab-based combinations** in patients with **untreated MM**. **Patients** with normal hepatic function and HI **could benefit** from treatment. Application of **subgroup analysis** should be considered with **caution**.

REFERENCES AND/OR ACKNOWLEDGEMENTS

¹Sun X, et al. How to use a subgroup analysis: users' guide to the medical literature. JAMA. 2014;311(4):405-11

²Gil-Sierra MD, et al. Checklist for clinical applicability of subgroup analysis. J Clin Pharm Ther. 2020;45(3):530-8.