soho2023
ELEVENTH ANNUAL MEETING

TREATMENT EFFICACY FOR RELAPSED AND REFRACTORY MULTIPLE MYELOMA (RRMM) PATIENTS WITH GAIN/AMPLIFICATION 1Q21: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

Xia Zhou[1]*, Hongying Wu[1], Lumei Hao[1], Liyan Wei[1], Xuemei Li[1], Junjing Yin[1], Qianru Yu[1], Zhanzhi Xie[2], Yuping Zhong[1]

1.Hematology Department, Qingdao Hospital, University of Health and Rehabilitation Science (Qingdao Municipal Hospital), Qingdao, Shandong, China;

2.Sanofi-Aventis China Investment Co., Ltd., Beijing, China.

INTRODUCTION

- Multiple myeloma (MM), the second most common haematologic malignancy (around 10%), is characterised by the proliferation and malfunction of plasma cells in the bone marrow[1].
- Gain/amplification of 1q21 (1q21+) has an increasing incidence and was detected in a higher proportion of relapsed or refractory MM (RRMM) (about 70%) than newly diagnosed MM (NDMM) (about 40-50%) [2,3].
- Several trials demonstrated that 1q21+ was associated with poor prognosis, drug resistance, and disease progression in NDMM and RRMM [3,4,5].
- The systematic review and meta-analysis of randomised controlled trials to evaluate the effectiveness of treatment regimens for RRMM with 1q21+.

METHOD

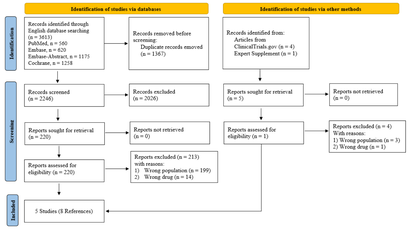
- We searched PubMed, EMBASE and the Cochrane Central Database.
- Randomised controlled trials (RCTs) comprised of patients with a diagnosis of RRMM of 1q21+ population who were 18 years old or older were considered.
- We included patients who were treated with: **A.**Anti-CD38 mAbs: Daratumumab (dara) and Isatuximab (Isa). **B.** Exportin-1 (XPO1) inhibitor: Selinexor. **C.** Antibody-drug conjugate (ADC): Belantamab. **D.** Anti-SLAMF7 mAbs: Elotuzumab (E). **E.** PIs: Ixazomib (I) and Carfilzomib (K). **F.** IMiDs: Pomalidomide (P).
- The primary outcome was progression-free survival (PFS). The secondary outcomes included overall survival (OS), overall response rate (ORR).

RESULTS

Characteristics of included RCTs

- The study selection process is shown in Figure 1.
- 5 RCTs were included by searching PubMed, EMBASE, and the Cochrane Central Database.
- A total of 2094 patients were included, with 926 of them were 1q21+ (44.2%). The median age ranged from 63 to 69 years old.

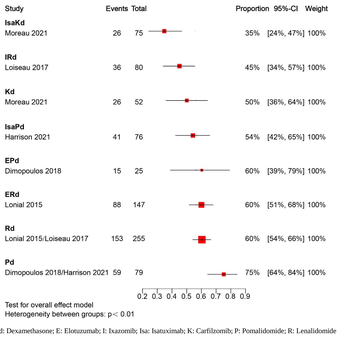
Figure 1 The PRISMA flow chart of study selection



Efficacy: Progression-free survival (PFS)

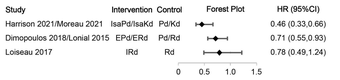
- The proportion ranged from 35% (95% CI 24% - 47%) in IsaKd to 75% (95% CI 64% - 84%) in Pd in Figure2.
- IsaPd or IsaKd lowered 54% of the risk of progression or death compared to Pd or Kd alone in Figure3.
- EPd or ERd lowered 29% of the risk compared to Pd or Rd alone in Figure3.
- The addition of Ixazomib lowered 22% of the risk compared to Rd alone in Figure3.

Figure 2 The proportion of progression-free survival (PFS) in various treatment regimens.



d: Dexamethasone; E: Elotuzumab; I: Ixazomib; Isa: Isatuximab; K: Carfilzomib; P: Pomalidomide; R: Lenalidomide

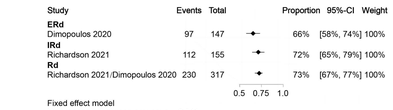
Figure 3 Forest plot for hazard ratio (HR) for progression-free survival.



Efficacy：Overall survival (OS)

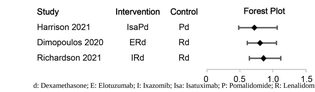
- The proportion of OS ranged from 66% in ERd to 73in Rd in Figure4.
- HRs (95% CI) of ERd and IRd showed no significant differences compared with Rd, with respective values of 0.81 (0.61 – 1.06)and 0.86 (0.66 – 1.12) in Figure 5.
- HR (95% CI) for OS of IsaPd showed no significant difference compared with Pd (HR 0.72, 95% CI 0.48 – 1.07) in Figure 5.

Figure 4 The proportion of overall survival (OS) in various treatments.



d: Dexamethasone; E: Elotuzumab; I: Ixazomib; R: Lenalidomide.

Figure 5 Forest plot for hazard ratio (HR) for overall survival (OS).

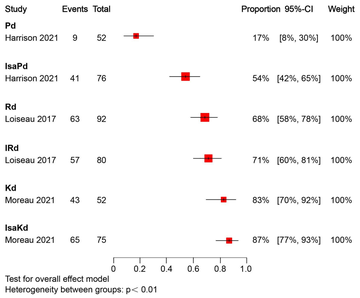


d: Dexamethasone; E: Elotuzumab; I: Ixazomib; Isa: Isatuximab; P: Pomalidomide; R: Lenalidomide.

Efficacy: Overall response rate (ORR)

- The proportion of ORR ranged from 17% (95% CI 8% - 30%) in Pd to 87% (95% CI 77% - 93%) in IsaKd in Figure 6.
- A higher ORR was observed in IsaPd compared to Pd in one study (n = 48, 51.9% vs. 9.5%, p = 0.0011) [6].

Figure 6 The proportion of overall response rate (ORR) in various treatment regimens.



CONCLUSIONS

- This study supports Isa-Pd or Isa-Kd have the beneficial effect for RRMM patients with 1q21+ compared to Pd or Kd regimens.
- This finding indicated that Isatuximab combination regimens have a beneficial tendency compared to other regimens, such as Ixazomib and Elotuzumab combination regimens.
- Well-designed trials are needed to make treatment recommendation for RRMM patients with1q21+.

ACKNOWLEDGEMENTS

Medical Writing support was provided by Havas funded by Sanofi and reviewed by Yuping Zhong. The authors are solely responsible for all content and editorial decisions.

FUNDING AND CONFLICT OF INTEREST

Funding: The study is supported by Sanofi.

Conflict of interest: Zhanzhi Xie is Sanofi employee and may hold shares and/or stock options in the company. Xia Zhou, Hongying Wu, Lumei Hao, Liyan Wei, Xuemei Li, Junjing Yin, Qianru Yu, Zhanzhi Xie, Yuping Zhong have nothing to disclosure.

CONTACTINFORMATION

Yuping Zhong, Hematology Department, Qingdao Hospital, University of Health and Rehabilitation Science(Qingdao Municipal Hospital) 266000, Tel:17669757939 Email: zhongyp3352@126.com.

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