mobilizados com fator estimulador de colônia de granulocitos (G-CSF). O RNA foi obtido utilizando-se o *RNeasy Mini Kit* (Qiagen, CA, EUA) e o transcriptoma analisado pelo sistema *GeneChip Exon Humano 1,0 ST Array* (Affymetrix, CA, EUA). Analisados com o *software Partek®* (http://www.partek.com) e pelo programa Metacore/portal Genego (Thomson Reuters), elencando vias superexpressas maior ou igual a 2 vezes (*Up regulation ou down regulation*). Foi selecionada para validação a via de sinalização redox e estresse oxidativo, analisando o produto de leucoaférese de 11 pacientes nas mesmas condições acima citadas. O perfil redox foi obtido através da avaliação de níveis circulantes de hidroperóxidos induzido por Butil (QL) e o perfil antioxidante medido através da capacidade antioxidante total (TRAP), ambos pela técnica de quimioluminescência de alta sensibilidade em tempo real. Foi calculado o índice de estresse através da relação pró/antioxidante. Os dados foram analisados no *software OriginLab* 9.0 e as comparações feitas no *software GrapPadPrism* 7.0 ($p \leq 0,05$). **Resultados:** No perfil global não foram observadas diferenças significantes em relação à comparação dos perfis pró e antioxidante dos pacientes vivos versus óbitos, sendo a média de QL (2094539,429 e 2173588,75), do TRAP (1,409 e 1,281) e índice de estresse (1672569,885 e 2016150,010), óbitos e vivos respectivamente. No transcriptoma, as principais vias associadas aos genes diferencialmente expressos foram inflamação e resposta imune, estresse oxidativo e neuroimunomodulação. No grupo óbito observou-se que a capacidade antioxidante de células tronco de pacientes portadores de plasmocitoma foi 50% menor que no grupo sem plasmocitoma. Não foram observadas diferenças no perfil de estresse em relação ao padrão de resposta ao tratamento (parcial x completa). **Discussão:** é bem documentado que mudanças no balanço redox de células tronco podem causar o estresse oxidativo. O balanço redox é potencializador de quimiorresistência pela alteração na indução de apoptose, sendo alterado por algumas substancias. Um exemplo controverso é a glutationa (GSH) que age como antioxidante mas sem papel definido no prognostico final do paciente com MM. Já na presença do plasmocitoma, sabemos que ele se expande mediado por citocinas secretadas por plasmócitos malignos, e pode estar relacionada com o aumento do estresse oxidativo versus óbito. **Conclusão:** Até onde sabemos, este é o primeiro estudo com foco em análise do perfil redox de células tronco de pacientes com MO. Os achados permitem concluir que existem variações no perfil de estresse oxidativo das células tronco em relação à presença de plasmocitoma no grupo óbito, sem variações para os demais perfis analisados e sem diferença nas comparações entre vivos e óbitos, sugerindo que o estresse oxidativo pode estar implicado neste modelo em situações específicas.

https://doi.org/10.1016/j.htct.2020.10.438

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ISATUXIMAB PLUS CARFILZOMIB AND DEXAMETHASONE VS CARFILZOMIB AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (IKEMA): INTERIM ANALYSIS OF A PHASE 3, RANDOMIZED, OPEN-LABEL STUDY

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Objective: To demonstrate benefit of adding Isatuximab (Isa) to (Kd) vs Kd in relapsed/refractory multiple myeloma (RRMM). **Methods:** In this Phase-3 study (NCT03275285), patients with RRMM and 1-3 prior lines of therapy were randomized 3:2 and stratified by number of prior lines and R-ISS to receive Isa-Kd or Kd. Isa-Kd arm received Isa (10 mg/kg IV) weekly for 4 weeks, then every 2 weeks. Both arms received K (20 mg/m^2 days 1-2, 56 mg/m^2 thereafter) twice-weekly for 3 of 4 weeks, and d (20 mg) twice-weekly. Treatment continued until disease progression or unacceptable adverse events (AE). Primary objective: increase in PFS of Isa-Kd vs Kd, determined by an Independent Response Committee (IRC). Comparison between arms conducted through log-rank testing. Key secondary objectives: overall response rate (ORR), rate of very good partial response (VGPR) or better, complete response (CR) rate, MRD negativity-rate (105 by NGS), and overall survival (OS). Key secondary endpoints tested with a closed test procedure. Safety data included treatment emergent adverse events (TEAE), hematological, and biochemistry results for all patients. Interim efficacy analysis was planned once 65% of total expected PFS events were observed. **Results:** 302 patients (Isa-Kd: 179, Kd: 123) were randomized. Median age 64 (33-90) years; R-ISS I, II, III was 25.8%, 59.6%, 7.9% respectively; 44%, 33% and 23% had 1, 2 and ≥3 prior lines respectively; 90% and 78% had prior proteasome inhibitor and IMiD respectively; 24% had high-risk cytogenetics. At a median follow-up

of 20.7 months and with 103 PFS events per IRC, median PFS was not reached for Isa-Kd vs 19.15 months Kd; HR 0.531 (99% CI 0.318-0.889), one-sided p = 0.0007. Thus, the pre-specified efficacy boundary (p = 0.005) was crossed. PFS benefit was consistent across subgroups. ORR (≥PR) was 86.6% Isa-Kd vs 82.9% Kd, one-sided p = 0.1930. ≥VGPR rate was 72.6% Isa-Kd vs 56.1% Kd, p = 0.0011. CR rate was 39.7% Isa-Kd vs 27.6% Kd. MRD negativity-rate (10-5) in ITT was 29.6% (53/179) Isa-Kd vs 13.0% (16/123) Kd, descriptive p = 0.0004. OS was immature (events 17.3% Isa-Kd vs 20.3% Kd). 52.0% Isa-Kd vs 30.9% Kd pts remain on treatment. Main reasons for treatment discontinuation were disease progression (29.1% Isa-Kd vs 39.8% Kd) and AEs (8.4% Isa-Kd vs 13.8% Kd). Grade ≥3 TEAEs were observed in 76.8% Isa-Kd vs 67.2% Kd. Treatment-emergent SAEs (59.3% vs 57.4%) and fatal TEAEs were similar in Isa-Kd and Kd (3.4% vs 3.3%,) and Infusion reactions were reported in 45.8% (0.6% grade 3-4) Isa-Kd and 3.3% (0% grade 3-4) Kd. Grade ≥3 respiratory infections (grouping): 32.2% Isa-Kd vs 23.8% Kd. Grade ≥3 cardiac failure (grouping): 4.0% Isa-Kd vs 4.1% Kd. As per lab results, grade 3-4 thrombocytopenia and neutropenia were reported in 29.9% Isa-Kd vs 23.8% Kd and 19.2% Isa-Kd vs 7.4% Kd, respectively. **Conclusion:** Addition of Isa to Kd provided superior, statistically-significant improvement in PFS with clinically meaningful improvement in depth of response. Isa-Kd was well tolerated with manageable safety and favourable benefit-risk profile, and represents a possible new standard of care treatment in patients with relapsed MM. Data first presented at EHA 2020 virtual meeting, June 11-21st. Study sponsored by Sanofi.

https://doi.org/10.1016/j.htct.2020.10.439

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ISATUXIMAB PLUS POMALIDOMIDE AND DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND SOFT-TISSUE PLASMACYTOMAS: ICARIA-MM SUBGROUP ANALYSIS

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Aim: To assess the efficacy and safety of treatment with Isatuximab-Pomalidomide plus dexamethasone (Isa-Pd) compared with Pd in patients with relapsed/refractory multiple myeloma (RRMM) and pre-existing plasmacytomas. **Methods:** 307 RRMM patients were randomized to two study arms (NCT02990338): Isa-Pd (n = 154) or Pd (n = 153). Isa was administered intravenously at 10 mg/kg weekly for 4 weeks, and every other week thereafter. If soft-tissue plasmacytomas were present at study entry, a computed tomography (CT) scan or magnetic resonance imaging (MRI) was carried out at baseline and repeated every 12 ± 1 weeks, and when clinically indicated. Imaging results were submitted to central radiology review as part of the independent review committee assessment. The primary objective was to assess the impact of Isa-Pd on the progression free survival (PFS) compared with Pd. Safety information including treatment-emergent adverse events (TEAEs) was assessed according to National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) version 4.03. **Results:** At study entry, soft-tissue plasmacytomas were present in 24 (7.8%) patients (14 [9.1%] in the Isa-Pd and 10 [6.5%] patients in the Pd arm). Baseline characteristics of patients with plasmacytomas included: median age, 61 (range 36, 82) years in the Isa-Pd arm vs. 64 (42, 71) years in the Pd arm; median (range) number of prior regimens before study entry, 3.5 (2, 13) in the Isa-Pd arm vs. 5.5 (2, 6) in the Pd arm; International Staging System, Stage I 50.0%, Stage II, 21.4% and Stage III, 28.6% in the Isa-Pd arm vs Stage I 10.0%, Stage II, 50.0% and Stage III, 40.0% in the Pd arm; high-risk cytogenetics, 21.4% in the Isa-Pd vs. 10% in the Pd arm. PFS was improved by adding Isa to Pd: hazard ratio: 0.22, 95% confidence intervals (CI): 0.07, 0.69. Median PFS was 4.57 (95% CI: 2.40, not calculable [NC]) months in the Isa-Pd arm vs. 1.56 (95% CI: 0.95, 4.47) months in the Pd arm. The probability of PFS at 12 months was 0.31 (95% CI: 0.10, 0.56) in the Isa-Pd arm vs. 0.00 (95% CI: NC, NC) in the Pd arm. The overall response rate (ORR) also improved with 50% (7/14) and 10% (1/10) responders in the Isa-Pd and Pd arms, respectively. Very good partial response (VGPR) occurred in 21.4% (3/14) of patients in the Isa-Pd arm and 10% (1/10) of patients in the Pd arm. Two patients with VGPR in the Isa-Pd arm who presented with plasmacytomas at baseline showed complete remission at cycle 3 and