651.MYELOMA: BIOLOGY AND PATHOPHYSIOLOGY, EXCLUDING THERAPY | NOVEMBER 13, 2019

Tumor Circulating Plasma Cells Detected By Flow Cytometric Single Platform Method Correlate with Clinical Response to Therapy and Unfavorable Patients' Characteristics

Vittorio Emanuele Muccio, Milena Gilestro, Elona Saraci, Andrea Capra, Alessandro Costa, Marina Ruggeri, Simona Caltagirone, Daniela Oddolo, Chiara Mussatto, Pellegrino Musto, Lucia Pantani, Vincenzo Pavone, Sonia Ronconi, Iolanda Donatella Vincelli, Anna Maria Cafro, Claudia Cellini, Vanessa Innao, Eugenio Piro, Francesca Gay, MD, Mario Boccadoro, Paola Omedé

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Background: In multiple myeloma (MM), different clinical parameters and molecular prognostic factors can predict disease course and response to therapy. The classification of myeloma patients includes laboratory parameters associated with higher tumor activity, resistance to therapy and proliferative competence. Tumor circulating plasma cells (TCPC) in MM patients showed a strong correlation with a more aggressive disease.

Aim: For the first time, we quantified the amounts of TCPC with single platform flow cytometric method and evaluated their relationship with patients' baseline characteristics and response to therapy before maintenance.

Methods: Whole peripheral blood samples from 413 newly diagnosed MM patients ≤65 years enrolled in the UNITO-MM-01/FORTE trial were collected. Patients were randomized [1:1:1; stratification: International Staging System (ISS) and age] to ARM A: carfilzomib-cyclophosphamide-dexamethasone (KCyd) followed by melphalan 200 mg/m^2 and autologous stem-cell transplantation (MEL200-ASCT) and consolidation with 4 KCyd; ARM B: carfilzomib-lenalidomide-dexamethasone (KRd) followed by MEL200-ASCT and 4 KRd; ARM C: 12 KRd cycles. Enrollment was completed in March 2017; data cut-off was November 30, 2018. For the single platform tube, the antibody combination CD38PC7/CD138PC5.5/CD45KO/CD56PE/CD19PB was mixed with 100µL of EDTA peripheral blood, dispensed with reverse pipetting, and incubated for 15 min, added with 500µL of lysing solution and, after 15 min, 100µL of flow count fluorospheres were dispensed with reverse pipetting and cells acquired with Navios flow cytometer. Intracytoplasmic tube was set up to confirm the clonality of CPC.

Results: Circulating plasma cells (CPC) were quantified in 413 samples, with median values of 0.03% (range: 0-51%) and 2.37/mm^3 (range: 0-6272/mm^3). White blood cells were 5710/mm^3 (range: 1752-26102/mm^3); total events acquired 1285000 (range: 40000-2000000); median CPC events were 58 (range: 0-441000); cellular events acquired were 190000 (range: 4428-1300000).

In 390 out of 413 samples (94.4%), CPC were detected; 272 samples (66%) showed TCPC with a median of 1.24/mm^3 (range 0.06- 6272/mm^3).

Patients were sorted according to different baseline characteristics and the medians of absolute TCPC were compared. The most statistically significant differences (p<0.001) were: haemoglobin (Hb) <10 (12.9/mm^3) vs. ≥10 (0.81/mm^3); ISS I (0.30/mm^3) vs. ISS II (2.85/mm^3) vs. ISS III (5.14/mm^3); R-ISS I (0.25/mm^3) vs. II (2.76/mm^3) vs. III (7.45/mm^3); albumin <3.5g/dL (2.76/mm^3) vs. ≥3.5g/dL (1.05/mm^3); β2-microglobulin <3.5mg/dL (0.67/mm^3) vs. 3.5mg/dL-5.5mg/dL (3.88/mm^3) vs. >5.5mg/dL (16.47/mm^3); lactate dehydrogenase (LDH) ≤upper limit of normal (ULN, 1.14/mm^3) vs. >ULN (7.36/mm^3); plasma cells (PC) in biopsy <60% (0.60/mm^3) vs. ≥60%(2.76/mm^3); with (3.18/mm^3) vs. without amp1q (1.18/mm^3); Morgan risk standard (1.21/mm^3) vs. high (3.00/mm^3).

Finally, we compared the absolute number of TCPC and the quality of response at the end of consolidation therapy. Higher values of TCPC were related to worst response: <partial response (PR, 4.23/mm^3) vs. ≥PR (1.23/mm^3); <very good PR (VGPR, 2.91/mm^3) vs. ≥VGPR (1.20/mm^3); <complete response (CR, 1.95/mm^3) vs. ≥CR (1.09/mm^3); <stringent CR (sCR, 1.71/mm^3) vs. ≥sCR (1.00/mm^3), p<0.05.

Conclusions: Single-platform flow cytometry is a simple method to quantify TCPC, present in almost all peripheral blood from MM patients; a high number is related to poor clinical response to therapy and helps in identifying high-risk patients. Moreover, it allows the discrimination between normal and pathological plasma cell population in peripheral blood. However, a longer follow up is needed to evaluate how TCPC can affect survival in patients with MM.

Disclosures

Musto:*Amgen:* Honoraria; *Celgene:* Honoraria. **Gay:***Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Boccadoro:***Sanofi:* Honoraria, Research Funding; *Celgene:* Honoraria, Research Funding; *Amgen:* Honoraria, Research Funding; *Janssen:* Honoraria, Research Funding; *Novartis:* Honoraria, Research Funding; *Bristol-Myers Squibb:* Honoraria, Research Funding; *AbbVie:* Honoraria; *Mundipharma:* Research Funding. **Omedé:***Janssen:* Membership on an entity's Board of Directors or advisory committees.

OffLabel Disclosure:

This presentation includes discussion of off-label use of a drug or drugs for the treatment of multiple myeloma.

Topics: neoplasms, plasma cells, total cavopulmonary connection, autologous stem cell transplant, multiple myeloma, carfilzomib, dexamethasone, albumins, antibodies, biopsy

Author notes

* Asterisk with author names denotes non-ASH members.

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Gay et al., Blood, 2019

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Dianne Nicol et al., Genome Med, 2017

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