Highlights from IMW 2021

1-2 febbraio 2022
Bologna
Royal Hotel Carlton

Monica Galli

Terapia di Prima Linea del Paziente Candidato ad ASCT

ASCT: Singolo o Doppio?

Coordinatore Scientifico
Michele CAVO

Comitato Scientifico
Michele CAVO
Maria Teresa PETRUCCI

Disclosures

Honoraria from:

Bristol-Myers-Squibb
Celgene
Janssen
Sanofi
Takeda

Plenary Session on Newly Diagnosed MM: Current Treatment Approaches

Treatment of Newly Diagnosed MM Transplant Eligible: what is the optimal induction? by P. Moreau

ASCT in NDMM transplant eligible by M. Cavo

Consolidation Strategies for MM by P. Sonneveld

Maintenance Strategies for MM by H. Goldschmidt

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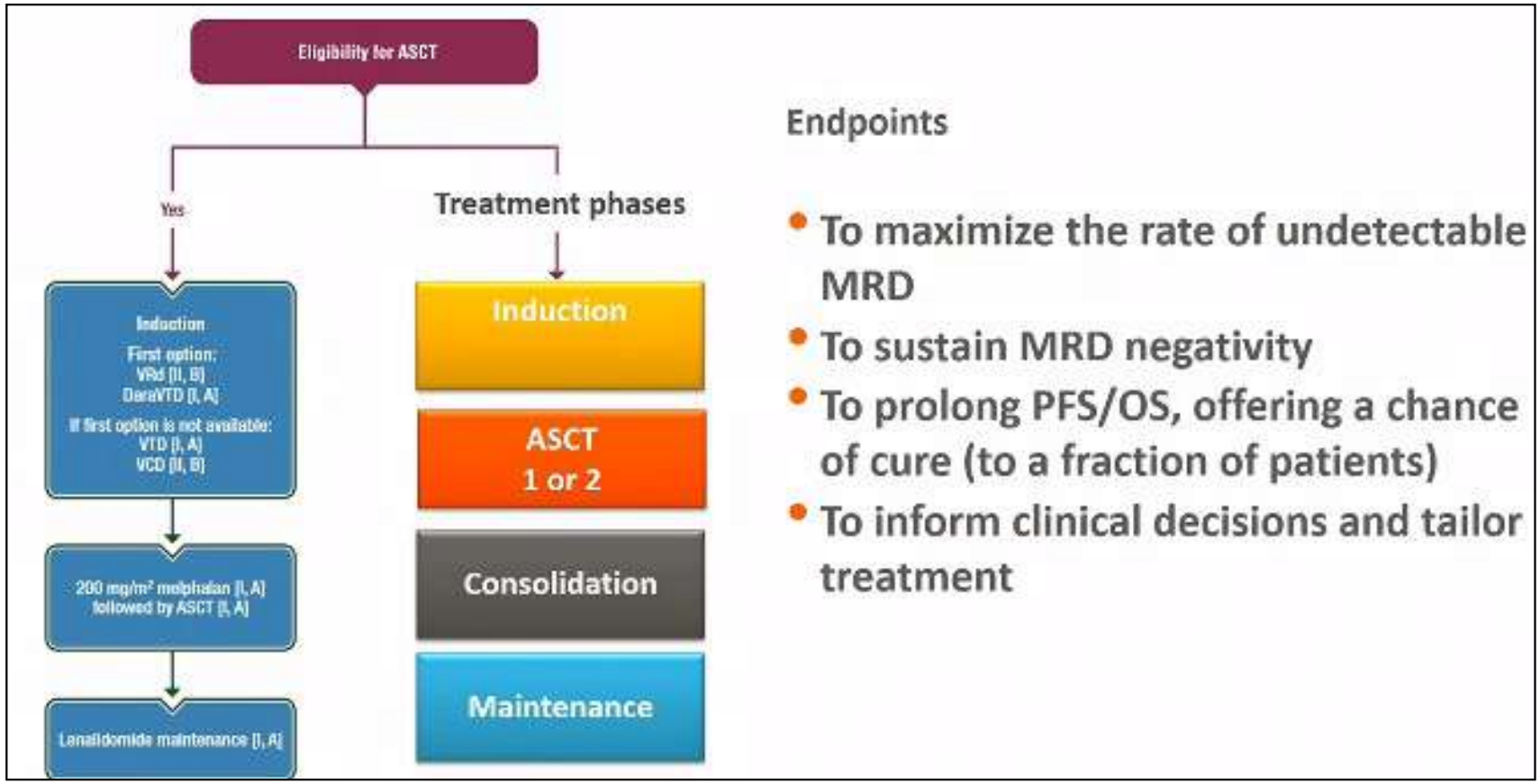
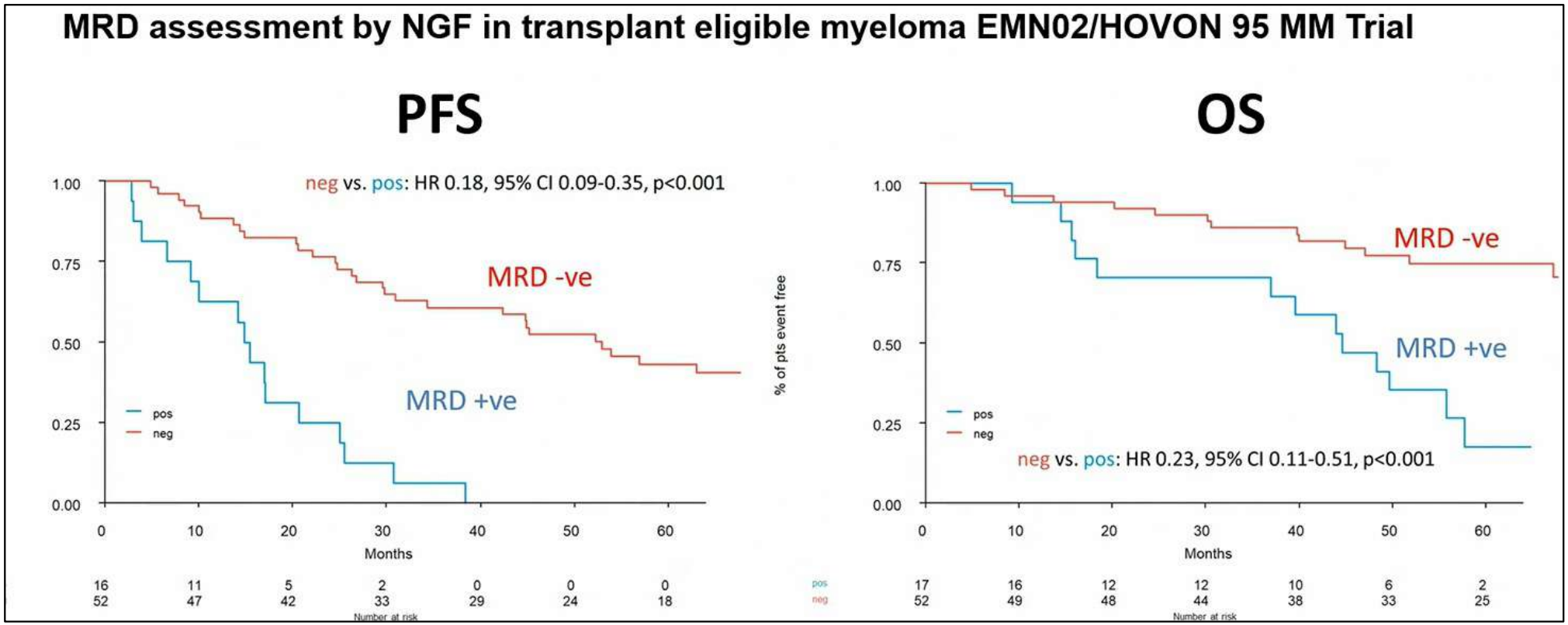
ASCT in Newly Diagnosed Multiple Myeloma



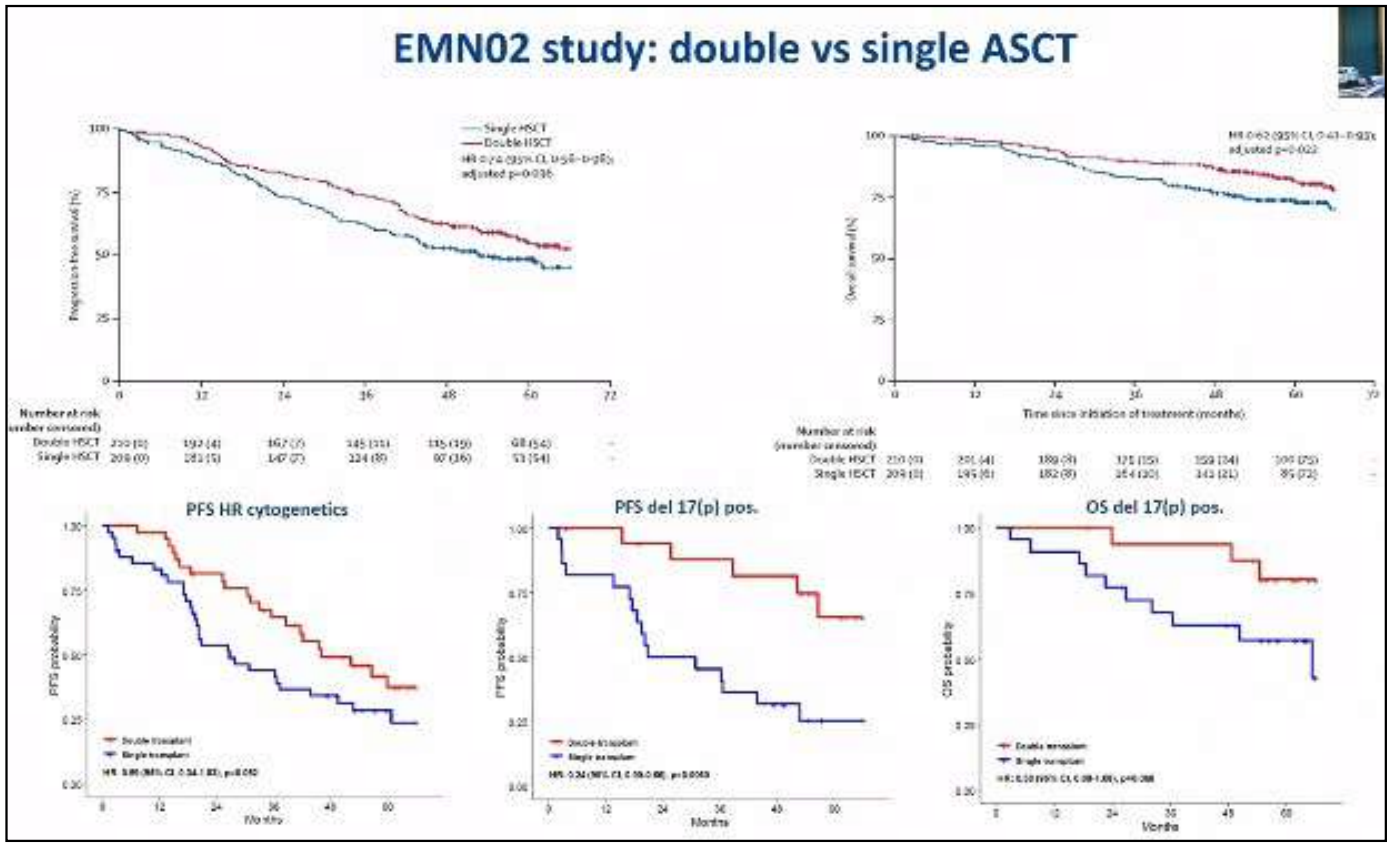
Michele Cavo. IMW 2021

MRD in ND TE Multiple Myeloma Patients



Oliva et al. Blood Cancer J 2021;11:106

ASCT in Newly Diagnosed Multiple Myeloma



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ASCT in Newly Diagnosed Multiple Myeloma

- **Upfront ASCT remains the reference treatment for fit patients with NDMM in the novel agent era**
- **Incorporation of novel drugs and drug combinations into the ASCT program has improved the rate of MRD negativity up to values of 50-60%**
  - similar, or even higher, unprecedented MRD negativity rates have been recently reported in patients treated with 4-drug regimens and no subsequent ASCT. Limitations: small series and short follow-up
- **Sustained MRD negativity is a challenge and a major requirement for cure**
- **MRD assessment at definite time points** to ask clinically-relevant questions
  - intensification or deintensification therapy in patients who are MRD-positive or negative
  - the ideal duration of maintenance post ASCT
- **Double ASCT:** the role is still debated

Michele Cavo. IMW 2021

Great Debates: Should Every TE NDMM Patient Receive a Transplant?

YES by S. Giralt

NO by M. A. Gertz

Great Debates: Should Every TE NDMM Patient Receive a Transplant?

NO by M. A. Gertz

- We need to stop thinking of SCT as the platform on which all myeloma therapy is built (transplant eligible is no longer question 1)
- Sct **is a regimen** and selection, and sequencing depends on availability of other regimens, reimbursement, trial access and availability of novel agents

Great Debates: Should Every TE NDMM Patient Receive a Transplant?

YES by S. Giralt

- High dose melphalan with autologous stem cell support as consolidation of initial therapy has been shown in multiple randomized trial to be associated with a significant PFS benefit.
- With long term follow up that PFS benefit can translate into a OS benefit and definitely a reduction in the burden of therapy and the need for new treatments.
- A priori, we cant identify who could benefir from HDM and thus all transplant eligible patients should receive it.
- Even patients with MRD negativity benefit from HDM and thus depth of response to induction should NOT be considered a reason not to proceed.
- POSSIBLE EXCEPTIONS
  - Low risk Stage 1 disease in a older patient (75 or older) MRD negative to induction.
  - Patients beyond one year of induction

Biologic Basis of the Impact of Autologous Hematopoietic Cell Transplantation in Multiple Myeloma Treated with Quadruplet Therapy

Background

Unprecedented depth of response is observed with quadruplet combinations in newly diagnosed multiple myeloma (NDMM). The incremental benefit of autologous hematopoietic cell transplantation (AHCT) in this setting has not been described and can be appraised with the serial assessment of minimal residual disease (MRD). Here we describe the impact of AHCT on MM burden assessed by next generation sequencing (NGS) for patients enrolled in the MASTER trial.

Methods

MASTER is a prospective, multi-center clinical trial utilizing daratumumab, carfilzomib, lenalidomide and dexamethasone (Dara-KRd) induction, AHCT (Melphalan conditioning), followed by MRD response-adapted Dara-KRd consolidation with planned enrichment for patients with high-risk chromosome abnormalities (HRCA). MRD assessment is performed by NGS (ClonoSEQ® platform) upon completion of induction therapy with 4 cycles of Dara-KRd, 60-80 days after AHCT and after each 4 cycle-block of consolidation, where applicable. Patients with confirmed MRD negativity (MRD$<10^{-5}$ in two consecutive time points) enter treatment free observation and active surveillance of MRD resurgence ("MRD-SURE"). The primary endpoint of the study is negativity utilizing IMWG criteria (MRD$<10^{-5}$). Achievement of MRD $<10^{-6}$ is an exploratory endpoint. Patients are categorized as having 0, 1, 2+ HRCA [gain 1q, t(4;14), t(14;16), t(14;20), del(17p)]. We describe changes in MRD burden with AHCT and explore patient and disease features influencing magnitude of MRD reduction with AHCT.

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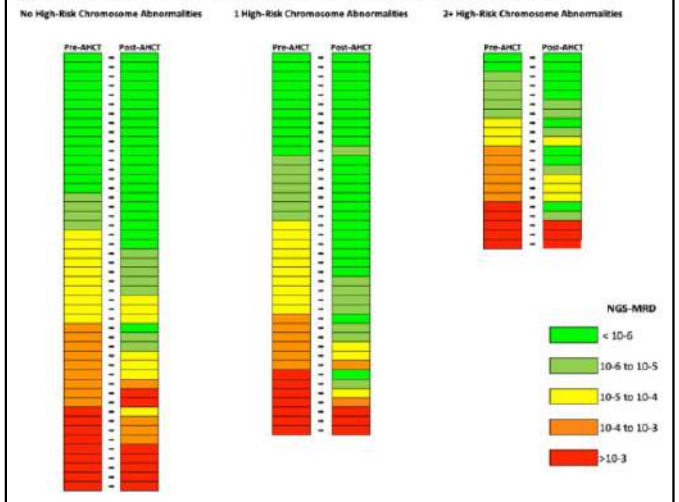
Biologic Basis of the Impact of Autologous Hematopoietic Cell Transplantation in Multiple Myeloma Treated with Quadruplet Therapy

Table – Proportion of patients reaching MRD<10-5 and <10-6 before and after AHCT according to cytogenetic risk

	MRD $<10^{-5}$ pre-AHCT	MRD $<10^{-5}$ post-AHCT	MRD $<10^{-6}$ pre-AHCT	MRD $<10^{-6}$ post-AHCT
No High-risk abnormality	40.4%	61.7%	31.9%	46.8%
1 High-risk abnormality	43.9%	78.0%	26.8%	61.0%
2+ High-risk abnormality	33.3%	66.7%	9.5%	42.9%
All patients	40.4%	68.8%	25.7%	51.4%

Figure – Changes in burden of MRD with AHCT according to cytogenetic risk



High-risk chromosome abnormalities: gain/amp 1q, t(4;14), t(14;16), t(14;20), del(17p)

Conclusions

An ultrasensitive quantitative MRD assay using NGS demonstrates the incremental benefit of AHCT in the context of highly efficacious quadruplet induction. The greatest impact is afforded to the highest risk disease subset elucidating the *biologic underpinnings* of the impact of AHCT in MM. At this time, AHCT should remain an integral part of therapy for fit, NDMM patients, particularly those with the high-risk disease and those who remain MRD positive after induction. Future studies exploring AHCT deferral in NDMM should be focused on patients who are MRD negative post optimal induction.

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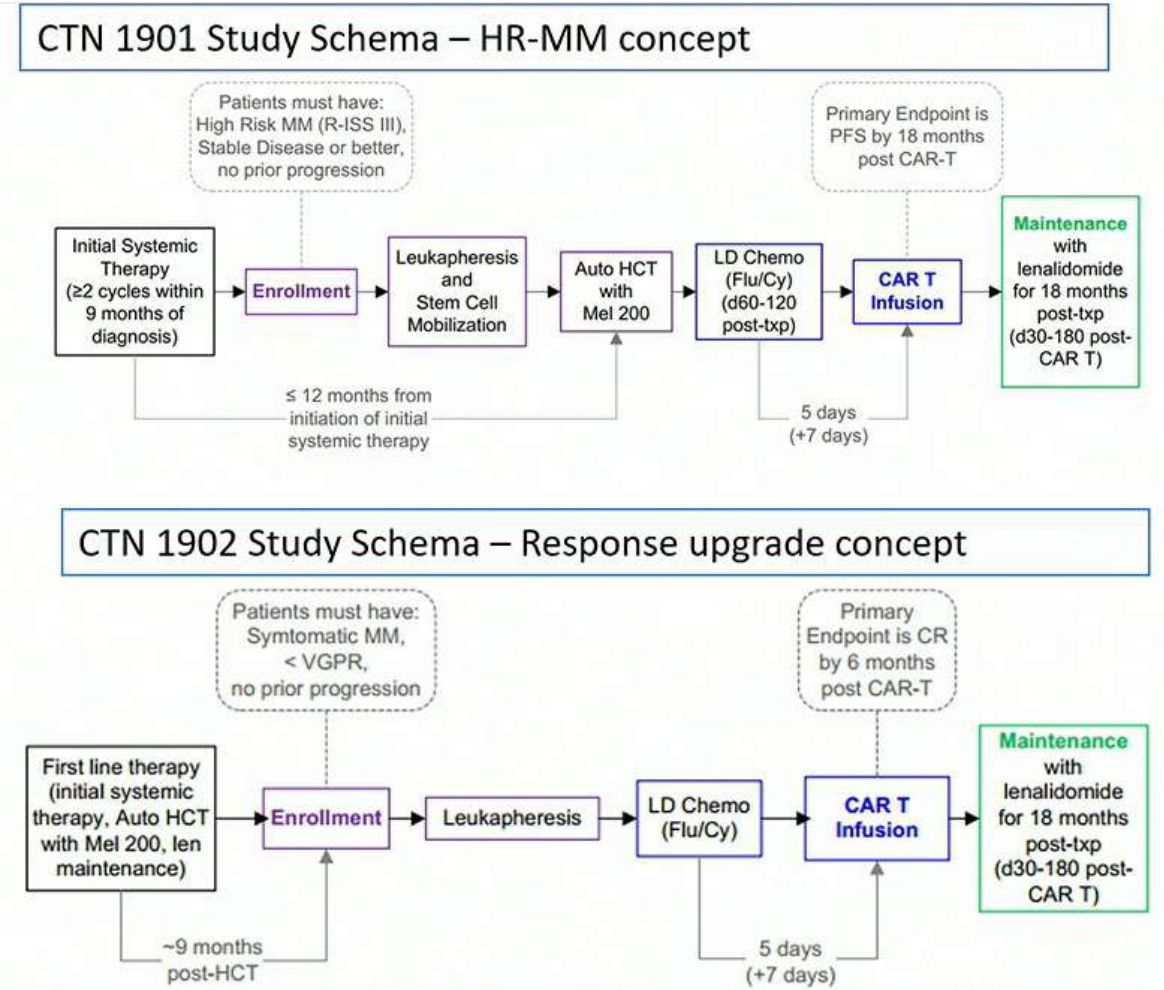

Tandem autoTx & CAR-T in High Risk Patients

Conclusions

AutoTx is going to stay as part of 1L treatment of young, transplant-eligible NDMM patients, because it improves the rate of MRD negativity, even in the novel drug era.

For the time being, double autoTx maintains a role in high risk patients; in the next future, it is problably going to be replaced by more modern treatment approaches, such as CAR-T.

Grazie dell'attenzione