My-DST Drug Assay to Optimize Therapy for Multiple Myeloma

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Background

- Multiple Myeloma is a malignancy of plasma cells accounting for ~10% of all hematologic cancers.1
- ~32,000 new cases of myeloma are diagnosed each year in the United States.2
- Therapy has evolved from traditional chemotherapy to monoclonal antibodies, proteasome inhibitors, and immunomodulatory drugs, often in addition to autologous stem cell transplant.3,4
- Treatment outcomes have improved but these new treatments are associated with potential toxicities and significant cost.
- Personalized treatment can be more efficacious and potentially avoid unnecessary side effects and costs.
- Multiple myeloma has broad genetic heterogeneity, many oncogenic drivers, and no targetable gene product making precision medicine challenging.
- Taking a phenotypic approach using ex vivo drug sensitivity profiling of tumor samples may lead to targeted personalized therapy, using only active agents, to minimize cost and toxicities.

Patient Case: 72 y.o. Male

- First developed back pain in sacrum radiating down both legs
- Lumbar x-ray suspicious for lytic bone lesion. Spine MRI with multiple myeloma with lytic bone disease
- ISS stage 1, R-ISS 1, SD 3a, normal karyotype, del13q (std risk)
- My-DST was performed on a sample donated by the patient which showed resistance to immunomodulatory drugs but sensitivity to proteasome inhibitors
- He was treated with four total lines of therapy (see table below)
- As predicted by My-DST, he had minimal response (MR) to the immunomodulatory agent Lenalidomide, but quickly achieved a very good partial response (VGPR) using bortezomib (proteasome inhibitor) and dexamethasone.
- This patient case was consistent with the My-DST assay results as he had an inadequate response to lenalidomide/dexamethasone
- This patient case demonstrates the potential benefit of personalized medicine in multiple myeloma treatment as the clinical course corresponded with ex vivo sensitivities.
- My-DST may be one method to improve outcomes for multiple myeloma through a more personalized approach.

Discussion

- Patients with multiple myeloma eventually relapse and become resistant to treatment.
- There are now many treatment choices, but response and side effects are often unpredictable.
- With multiple myeloma which affects primarily older patients with a median onset of 70 years, frailty and comorbidities are also important when discussing toxic treatments.1
- Elderly and frail patients are sometimes undertreated or overtreated leading to worse clinical outcomes. Personalized therapies and better drug selection may improve the response for this population.4
- This patient case demonstrates the potential benefit of personalized medicine in multiple myeloma treatment as the clinical course corresponded with ex vivo sensitivities.

Conclusions

- Multiple myeloma is a heterogeneous hematologic malignancy with an expanding array of treatments.
- A more optimized/personalized therapy selection approach would reduce exposure to potentially harmful agents with side effects, eliminate wasted time from ineffective agents, and reduce costs.
- This patient case was consistent with the My-DST assay results as he had an inadequate response to lenalidomide/dexamethasone but achieved a very good partial response when switched to bortezomib/dexamethasone.
- Further studies with My-DST need to be done to further evaluate the success of phenotypic-based therapy.

References


Acknowledgements

• Thank you to the patients who donated samples for the development of My-DST.
• This work was supported by grants from the Colorado Clinical & Translational Sciences Institute (Junior Faculty CO-Pilot Award, NIH/NCATS CTSA Grant Number UL1 TR002535) to D.W.S., the National Comprehensive Cancer Network (NCCN) Foundation (2016 Young Investigator Award) to D.W.S. and the National Cancer Institute (K08CA227014) to D.W.S. The authors would like to thank the Hematology Clinical Trials Unit at the University of Colorado for tissue bank and regulatory support.