High-Risk MDS Patient

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- 39 Y/O M
- Pancytopenia and fever for a year
- BM biopsy: MDS , 3% blasts , complex karyotype : -5q, del p53
- High risk MDS , IPSSR : 6
- Patient with somewhat intellectual disability, “funny” looking facial features, glaucoma, ataxia . No definite neurological diagnosis

- Family history :
- Mother and father are related (fourth-degree kinship)
- 2 sisters (1 sister had breast cancer, BRCA neg)
- Multiple malignancies (mostly breast) in the family

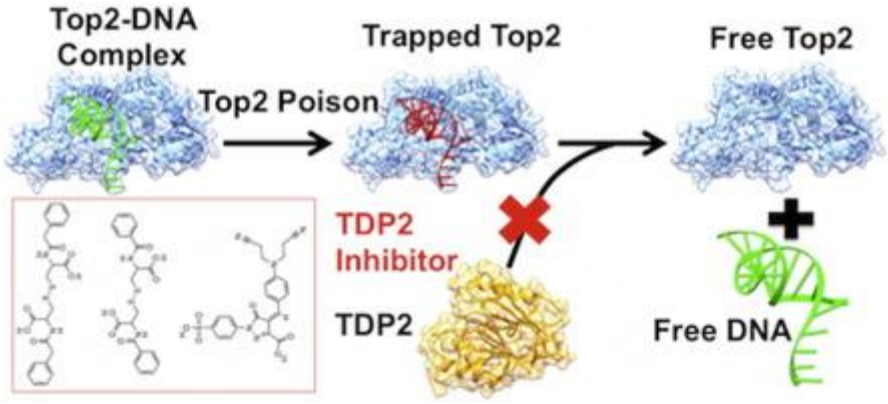
Should we proceed for allo-BMT ? Yes

Who are the potential allo-BMT donors of this patient?
Should we transplant one of his sisters in case of a match?
Or Search for MUD from the beginning ?

Genetic analysis

- Triple whole exome sequencing was sent for analysis
- Pediatric Hemato-oncologist also suspected syndromic appearance and advised against MSD for allo-BMT, our BMT team supported MUD
- Whole exome results : JAK2 positive heterozygote (maternal), TDP2 homozygote

What is TDP2 ?



- Topoisomerase2 participate in the unwinding of DNA during replication – causing transient breaks in DNA
- Topo 2 poisons like Etoposide prevents re-ligation if DNA
- TDP2 - Tyrosyl-DNA phosphodiesterase 2
- DNA strand break repair protein
- It is required to repair the accidental double-strand breaks produced by the abortive activity of Topoisomerase II

TDP2

- *TDP2* mutation in humans has been associated with intellectual disability, seizures, and ataxia.
- An ultra rare disease now denoted as spinocerebellar ataxia, autosomal recessive 23 (SCAR23) in children (5 patients described)
- Neutropenia was reported in 1 case
- MDS or other hematological malignancies not described

Discussion

- Back to basics: history taking, family history and Physical examination!
- When to perform whole exome ?
- Donor selection? MSD? MUD?
- Conditioning regimen ? Is he chemo-sensitive as Fanconi anemia?
- What is the impact of JAK2 heterozygote in this case?
- Is MDS a feature in older patients with SCAR23 disease not yet described?