The Future Landscape of Graft vs host disease (GVHD) prevention trials

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INTRODUCTION

- Graft vs host disease remains an important complication of allogeneic stem cell transplant and results in non-relapse mortality and significant morbidity to the patients who receive allogeneic stem cell transplant.
- The incidence of GVHD after allo-HSCT varies from 30-50% depending on the host, graft source, and other risk factors.
- The standard regimens for the prevention of graft vs host disease include methotrexate plus calcineurin inhibitors, with post-transplant cyclophosphamide being the most common regimen for haploidentical transplant based on the Johns Hopkins regimen.
- Multiple clinical trials are ongoing for the prevention of GVHD. We review the future landscape of clinical trials in the prevention of GVHD.

AIM

- We aim to find the design and endpoints of the clinical trials that are taking place in the GVHD prevention space to foresee the innovation and technological advances to prevent the important complication of allogeneic stem cell transplant.

METHODS

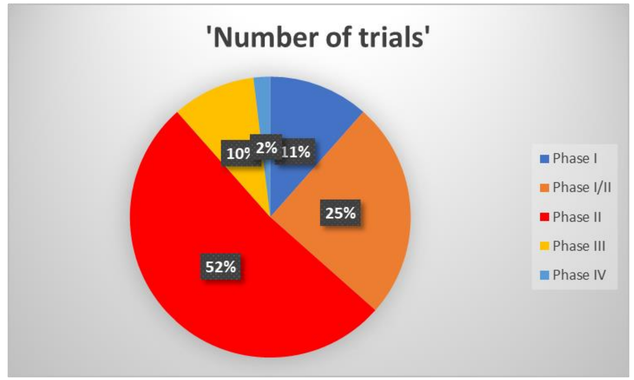
- We searched the clinical trial registration sites (clinicaltrial.gov, European clinical trial union, and Australia-New Zealand clinical trial network) with the terms “graft-vs-host-disease” and “prevention.”
- We included all the trials that are ongoing with completion dates after 05-01-2023.
- We excluded the trials that have been completed, withdrawn, or ended prematurely.
- We also excluded all the trials that have no updates for the last five years or the trials that were to be completed before 05-01-2023.

RESULTS

- We found 317 trials studying the graft vs host disease in the trial registries
- After the exclusion of duplicates and treatment-based trials, we extracted data from 52 trials.
- Most studies were in Phase II (n=27), while only five were in Phase III.
- The median number of patients in all the studies was 70 (12-540).
- The most common regimens being studied for GVHD prevention are post-transplant cyclophosphamide(n=25), JAK inhibitors (n=8), and abatacept (n=5).
- The most common primary endpoint was the incidence of GVHD (n=20). Nine studies had the primary endpoint of graft-free relapse-free survival (GRFS).
- Eight other studies included GRFS as a secondary endpoint.
- The quality of life as a secondary endpoint was included in two studies only.
- Overall survival was not primary endpoint for any study, but it was included in 29/52 studies
- Table 1 details the various study endpoints.

Table 1: Characteristics of the trials

Total number of trials	52
Total estimated enrolment	6380
Phase of clinical trial	
Phase I	6
Phase I/II	13
Phase II	27
Phase III	5
Phase IV	1
GVHD prophylaxis used	
ATG based	4
Abatacept	5
Post transplant cyclophosphamide	25
Tocilizumab	2
JAK inhibitor based (itacitinib, ruxolitinib, pacritinib	8
Others	13
Trial sites	
US/Canada	32
Australia	1
Europe	12
Asia	7
South america	1
Conditioning regimen	
MAC	11
MAC/RIC/NMA combination	8
RIC	10
Not specified	21
Study population	
aGVHD	15
cGVHD	5
Both	30
NA	2
End points	
GRFS	9
Incidence of GVHD	20
safety/toxicity/MTD	11
Other/composite	12



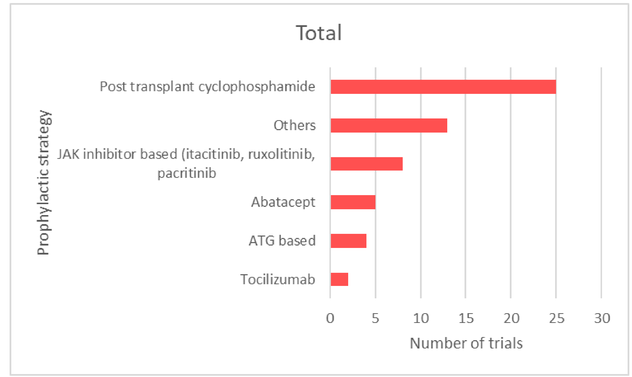


Figure 1 . Trials by phase Figure 2. Prophylactic strategies

CONCLUSIONS

- In our study, we found that post-transplant cyclophosphamide (PTCY) and JAK inhibition are the most used GVHD prophylactic regimens in currently ongoing clinical trials.
- There is a lack of uniformity in the endpoint reporting, and patient-reported outcomes are seldom represented in the ongoing clinical trials for GVHD prevention.
- Future studies with a focus on novel techniques, and uniform outcome reporting are needed.

REFERENCES

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