

Wrap-up

Steven Pavletic, MD
Experimental Immunology and
Transplantation Branch
National Cancer Institute

CIBMTR Survey on Treatment of Acute GVHD

- 59 Center Responded

Locations of responding centers:

North America	35
South America	6
Europe	9
Middle East	3
Pacific Rim	6

Preliminary results

CIBMTR Survey on Treatment of Acute GVHD

- Annual transplant volume

# BMTs	Adults	Peds
0	11	27
1-5	4	12
6-10	4	6
11-20	8	6
21-50	19	7
51-100	7	1
>100	6	0

Preliminary results

CIBMTR Survey on Treatment of Acute GVHD

	Yes	No	Unk
FACT or JACIE Acc'd?	32	27	0
SOP for A GVHD Treatment?	39	18*	2

*Twelve US centers reported not having an SOP for treatment of acute GVHD.

Preliminary results

CIBMTR Survey on Treatment of Acute GVHD

What is your standard treatment for adults with new gr 2-4 acute GVHD?¹

Regimen	MRD	MUD
Steroid 2 mg/kg/day ²	27	24
Steroid 1-2 mg/kg/day	3	4
Steroid 1 mg/kg/day	1	1
Steroid 2.5 mg/kg/day	1	0
High-dose steroid	1	1
Blank	6	9

¹Of the 39 responding that they had an SOP for GVHD treatment.

²Five centers indicated lower steroid dose for gr 2 skin alone, and six center indicated lower steroid dose for upper GI GVHD alone

Preliminary results

CIBMTR Survey on Treatment of Acute GVHD

What is your standard first salvage regimen for adults with acute GVHD?¹

Regimen	MRD	MUD
No Standard	11	11
Anti-IL-2R-based	9	7
MMF-based	6	7
ATG-based	7	6
Anti-TNF-based	5	6
High-dose steroid	1	2

¹Of the 39 responding that they had an SOP for GVHD treatment.

Preliminary results

**Public Workshop on Clinical Trial
Endpoints for Acute GVHD
After Allogeneic Hematopoietic Stem Cell
Transplantation
5/19/09**

Stated Objective

“To review the data that will serve as the **foundation for protocol design** and clinical trial **evidence-based** endpoints intended to **support the approval** of new drugs or biologics to prevent or treat acute GVHD”

“**inform FDA and assist investigators** in facilitating clinical development programs for products to prevent or treat acute GVHD”

What did we learn? (Pavletic)

	Prevention	Treatment
Does heterogeneity in eligibility matter?	Yes, very much so Age, conditioning, disease	Yes Age, disease, grade, match
Are diagnostic criteria established?	Yes, clinical criteria Biopsy ~ 60% sensitivity	n/a
Are there meaningful criteria for grading?	Grade III/IV (II-IV?) Reproducibility (collect raw data)	n/a
Are there meaningful criteria for response?	n/a	CR and PR (comparable) ?VGPR/CR
What EPs denote clinical benefit for full approval?	Grade III/IV, Survival	CR/PR (day 28 or 56) Survival
What EPs likely predict clinical benefit for AA?	Grade III-IV Grade II-IV (morbidity)?	CR/PR (day 28 or 56) (predict NRM, survival)
What is the role for biomarkers?	Identified candidates Need validation	Fewer clear candidates Need validation
What is the role for PROs?	Unlikely endpoints	Likely role - Symptoms are important

Timing and Symptoms of GVHD

Acute GVHD:

Red skin rash, GI symptoms, liver

Chronic GVHD

Skin, eyes, mouth, gastrointestinal, liver, musculoskeletal, lung, genitourinary



