

# Blood and Marrow Transplant Clinical Trials Network (BMT CTN)

*Improving therapies. Saving lives.*

## Request to Co-Fund

- ❖ Reissuance of RFA-HL-17-018 and RFA-HL-17-019
- ❖ Funded by NHLBI (lead IC) and NCI since 2001

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BSA-NCAB Joint Meeting

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# BMT CTN, a National Leader in Hematopoietic Stem Cell Transplantation (HCT) Trials

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Funded by NHLBI and NCI for 21 years



Unique Attributes:

- Phase II & III HCT & Adoptive Cell Therapy (ACT) trials for malignant and non-malignant blood disorders which can't be replicated elsewhere
- Multi-disciplinary, world leaders that have evolved to meet current medical research needs (e.g., CAR T cell therapy)
- Center membership enable outreach to underserved and minority communities (e.g., small medical centers, consortia, etc.)
- An open forum for research planning, strategy, and priority setting via State-of-the-Science Symposia (SOSS)
- Informs trial designs, clinical practice, and CMS national coverage determinations
- Leverages additional resources
  - ❖ NCTN, AIDS Malignancy Consortium, and Sickle Cell Disease Clinical Research Network
  - ❖ Industry and philanthropic collaborations

# BMT CTN Research and Accomplishments

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Disease Targets: leukemia, myelodysplasia, lymphoma, multiple myeloma, human immunodeficiency virus (HIV)-associated cancers

## Areas of Study

GVHD prevention, treatment, and disease biology

Graft sources

Conditioning regimens / maintenance therapy / comparison to non-HCT therapy

Rare and non-malignant diseases

Disease biology and control

Quality of life and patient experience

Cellular and gene therapy

## Overall Productivity (August 31, 2022)

- A. Trials Launched: 60; 52 relevant to NCI's mission
- B. Trials Completed: 35/31\*\*
- C. Trials Terminated: 3\*\*
- D. Trials Ongoing: 22/18\*\*
- E. Accrual Performance: 16,200 patients overall; 784 on NCTN Collaborative Studies. 7,500 current project period.
- F. Publications: 148 manuscripts including 38 primary results papers from 42 trials. 77 papers published since 2017.
- G. Sample Repository: 530,910

\*\*Data excludes NHLBI trials on aplastic anemia, sickle cell disease, and hemophagocytic syndromes

# Significant Findings and Impact (Example 1 – BMT CTN 0702)

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(1) Multiple Myeloma (MM):

- MM affects ~31,000 new patients in the US yearly; many will experience disease progression.

(2) BMT CTN 0702: Phase III Randomized Trial of Single Autologous Transplant with or without Consolidation versus Tandem Transplant and Maintenance Therapy for MM patients.

- Primary Objective: Compare progression-free (PFS) between the 3 treatment arms.
- Results: No difference in PFS or overall survival.

(3) SIGNIFICANCE: Showed that tandem transplantation does not improve outcome, thus favorably affecting public health expenditure (e.g., fewer tandems) and saving individual patients from added toxicity.

*Journal of Clinical Oncology. 2019 Mar 1;37(7):589-597.*

# Significant Findings and Impact (Example 2 – BMT CTN 1304)

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- (1) Dana Farber Cancer Institute 10-106/ BMT CTN 1304: Phase III Randomized Trial of Lenalidomide, Bortezomib, Dexamethasone (RVD) alone vs RVD plus High-Dose Treatment with Autologous HCT in MM (patients up to age 65).
  - Primary Objective: Compare PFS between the 2 arms.
  - Results: RVD plus AutoHCT was associated with longer PFS than the RVD alone. However, no overall survival (OS) benefit was observed.
- (2) SIGNIFICANCE: Demonstrated that with RVD therapy, transplant can be delayed without harm, thus creating the ability to individualize patient care.

*New England Journal of Medicine 2022 Jul 14;387(2):132-147.*

# NCI Program Evaluation Conclusions

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RATING: ***Outstanding to Exceptional*** progress. Its structure, organization, and operations are efficiently designed for developing, activating, and completing trials. Studies thus far have led to paradigm shifts in the management of leukemia and multiple myeloma - BMT CTN 1102, 0702, 1304, and 1902.

The BTM CTN:

- Is the only contemporary coalition of centers that performs clinical studies in HCT. Strength: ***scientific rigor and integrity*** of the leadership and its technical committees in terms of conceiving, designing, and implementing studies.
- Structure ensures a democratic and open process inviting input from all participating centers to effectively prioritize resources towards projects with ***the greatest yield*** in terms of scientific merit and feasibility.
- Demonstrated the ability to ***adapt to ongoing changes*** and evolution in existing treatment paradigms, such as the development and implementation of therapies such as CAR T-cell therapy and other immunotherapeutic agents.

RECOMMENDATION: Unanimously agreed to continue supporting a BMT CTN.

# Research Agenda for the Reissuance

## (RFA-HL-17-018 and RFA-HL-17-019)

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(1) Defined by the 2021 SOSS High Priority Topics:

- Improve engraftment, immune reconstitution, and evaluate emerging cellular therapies or engineered grafts designed to address specific complications of HCT.
- Prevent or reduce regimen related toxicities and relapse.
- Prevent or treat GVHD.

(2) Support 6 clinical trials and NCTN studies:

- **S2114:** "A Randomized Phase II Trial of Consolidation Therapy Following CD19 CAR T-Cell Treatment For Relapsed/Refractory *Diffuse Large B-Cell Lymphoma or Grade IIIB Follicular Lymphoma.*"
- **S2213:** "A Phase III, Randomized Study of Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone (Dara-VCD) Induction Followed by Autologous Stem Cell Transplant or Dara-VCD Consolidation and Daratumumab Maintenance in Patients with Newly Diagnosed AL *Amyloidosis.*"
- **EA4211:** "A Randomized Phase III Trial of Chemotherapy vs. Pembrolizumab Plus Chemotherapy for Relapsed/Refractory *Classical Hodgkin Lymphoma.*"

# NCI Budget Request: FY2024 to FY2030

Participating Institute	Total Costs for the Current Funding Cycle	Total Costs for the Proposed Reissuance
<b>NCI</b>	<b>\$27.3M</b>	<b>\$27.3M</b>
NHLBI	\$45.0M	\$53.8M
<i>Total Sum</i>	<i>\$72.3M</i>	<i>\$81.1M</i>

- NCI's Investment: Remains the same. Total costs of **\$3.9 million per year** for 7 years. Total **\$27.3M**.
- Number of Awards: 19 (1 DCC and 18 Core Clinical Sites funded via U24 and UG1 cooperative agreements respectively).
- Number of Years: 7
- NHLBI\* contributions: Gradient scale. \$53.8 million in total (66.3%).

\*Renewal request approved with an anticipated start date: September 1, 2024.



*Thank you for your attention!*



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