



Debate: Haploidentical (haplo) versus Umbilical Cord Blood (UCB) Transplant

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Objectives

1. Recognize the indications for alternative donor (umbilical cord blood, HLA-haploidentical related donor) transplantation.
2. Explain the relative risks and potential benefits of cord blood versus haplo transplantation.
3. Describe differences in the composition of umbilical cord blood versus human leukocyte antigen (HLA)-haploidentical bone marrow grafts.
4. Compare the toxicities of umbilical cord blood transplantation with those of HLA-haploidentical related donor stem cell transplantation.
5. Compare outcomes of reduced-intensity transplantation using cord blood with those using HLA-haploidentical bone marrow.
6. Distinguish relative advantages and disadvantages of these two graft sources.



Disclaimer

- Neither I nor anyone else knows which graft source, cord blood or HLA-haploidentical related donor stem cells, is better
 - This is why I am the co-principal investigator of a multi-center, phase III study comparing the two graft sources
- Results of cord blood transplantation in children are excellent





**“Whoever saves a life,
it is considered as if she
saved an entire world”**

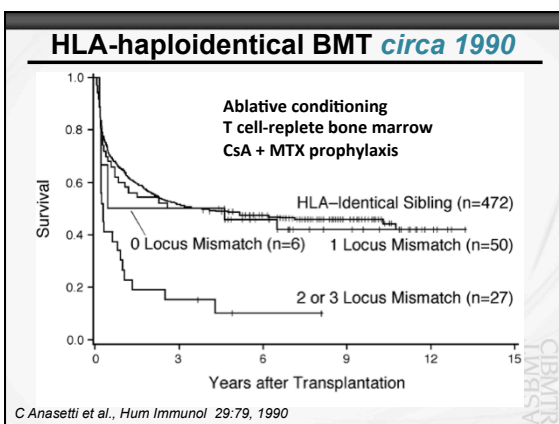
--Mishnah Sanhedrin 4:9;
Babylonian Talmud
Tractate Sanhedrin 37a

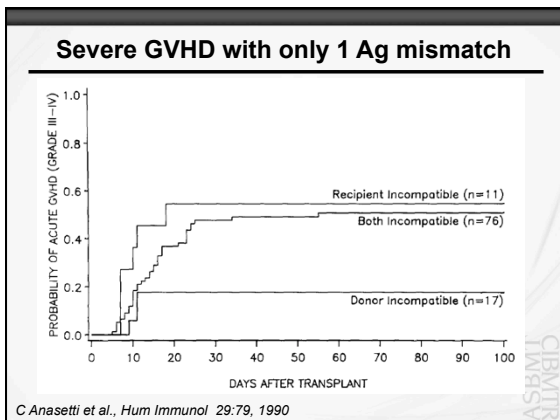
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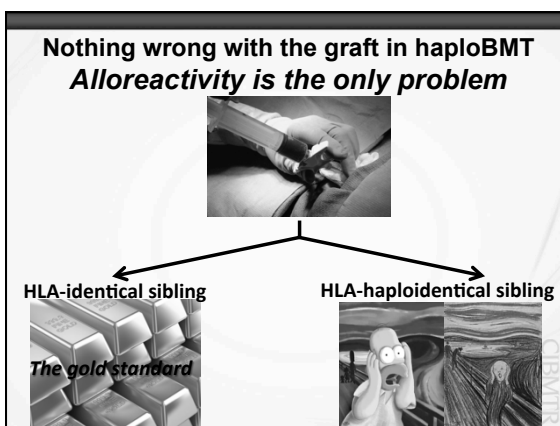
Why haplo is better than cord

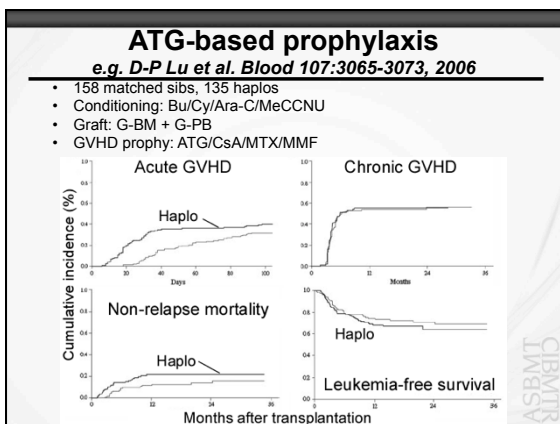
- The results of HLA-haploidentical transplants have improved dramatically and now approach those of HLA-matched transplants
 - Improved prophylaxis of GVHD and graft rejection
- UCB has inherent limitations as a graft source
 - Cost
 - Stem cell and total cell dose→poor engraftment
 - T cell dose and naïveté→poor immune reconstitution
 - Non-recurring cell source→no donor lymphocyte infusions
- Haplo opens up new possibilities
 - Combined bone marrow and solid organ transplantation

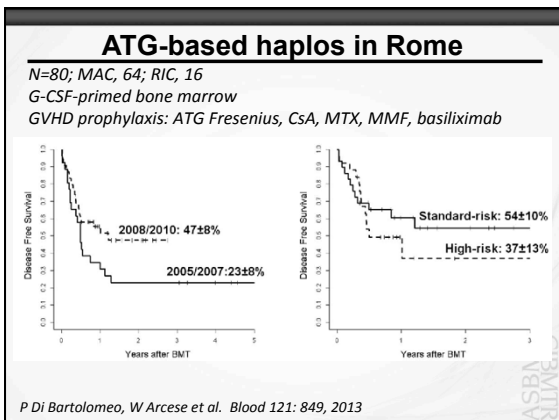
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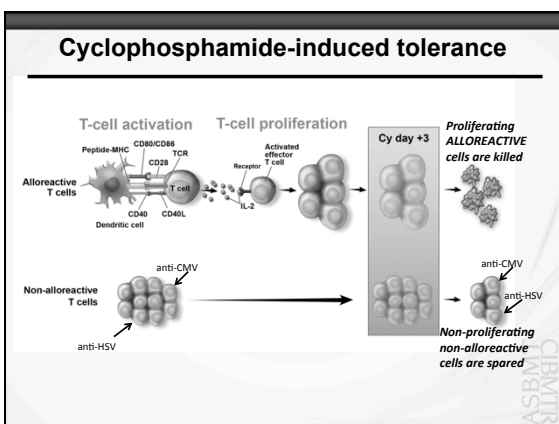


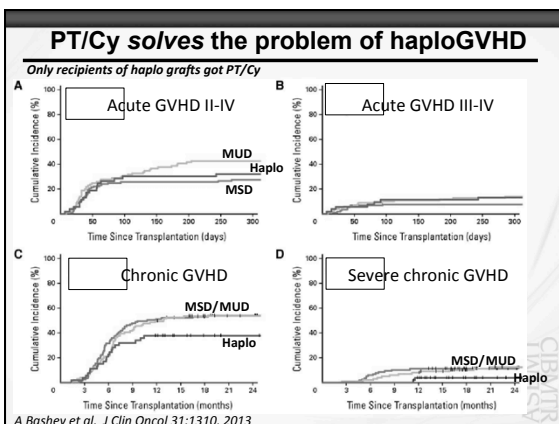


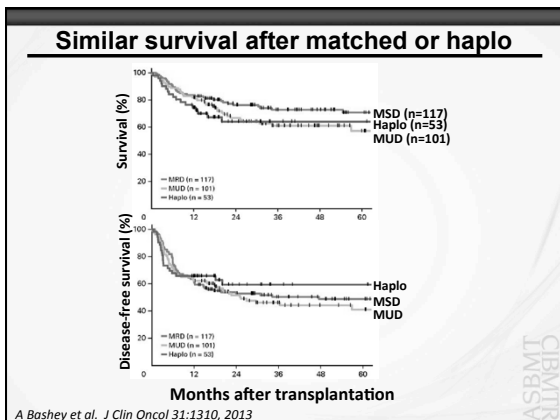








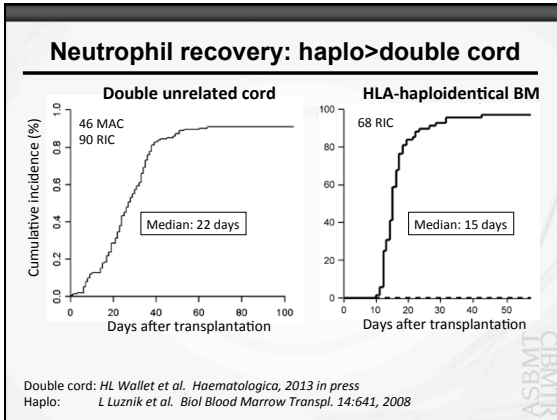


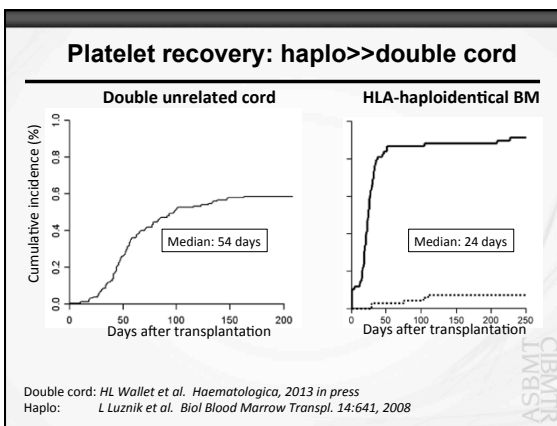


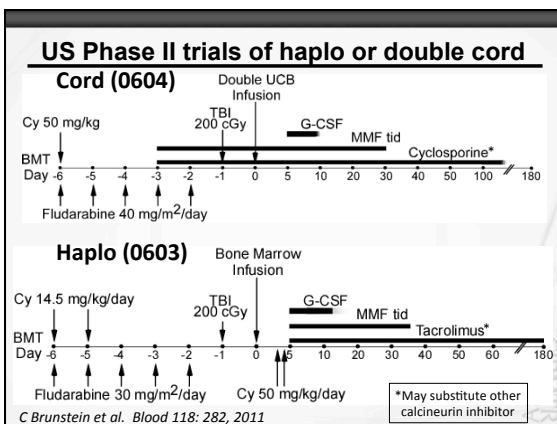
Question 1: In 2014, which GVHD prophylaxis regimen would be considered inadequate for T cell-replete, HLA-haploidentical BMT?

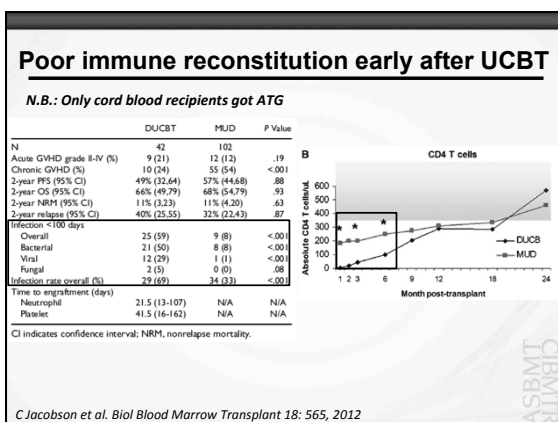
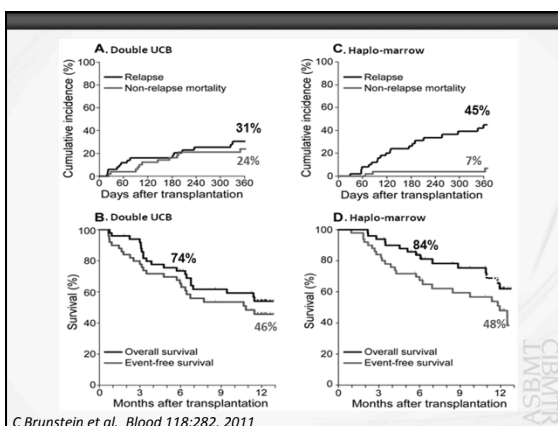
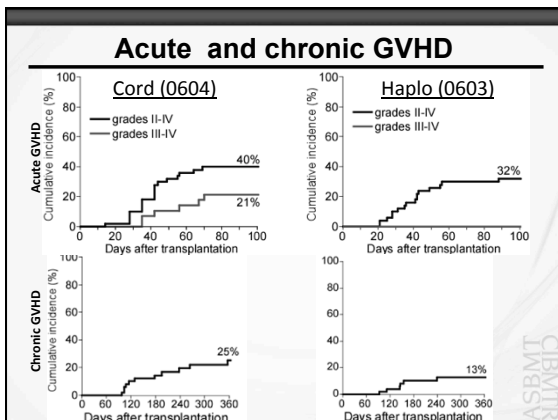
- A. Cyclophosphamide, tacrolimus, mycophenolate mofetil (MMF)
- B. ATG, cyclosporine (CsA), methotrexate, MMF
- C. CsA plus methotrexate (MTX)
- D. ATG, CsA, MTX, MMF, and basiliximab

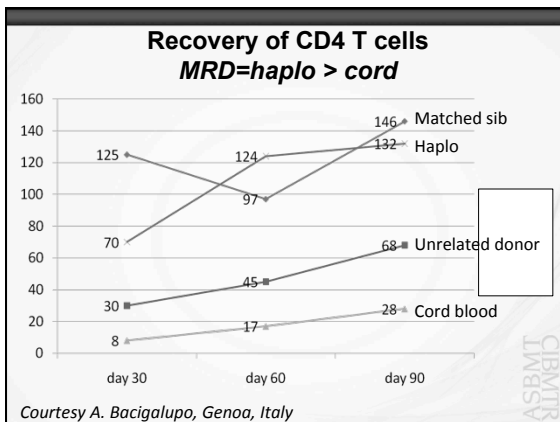
Haplo versus double cord after reduced intensity conditioning

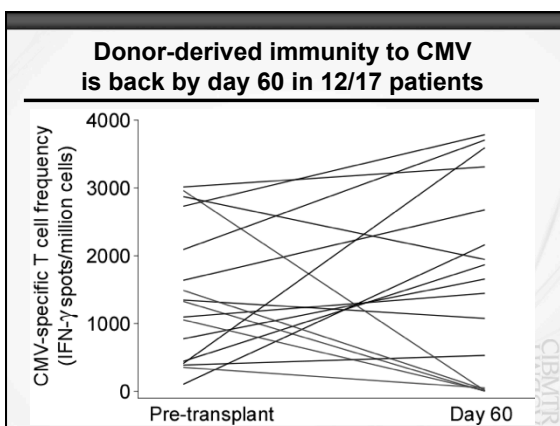












Cord blood: a luxury item

Country	GDP per capita	Population (million)
Qatar	\$102,800	1.9
Two cord blood units	~\$60,000	
USA	\$49,800	317
Germany	\$39,100	81
Brazil	\$12,000	201
China	\$9,100	1360
Indonesia	\$5,000	238
India	\$3,900	1235
Pakistan	\$2,900	185
Nigeria	\$2,700	174

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Assistant:
 "Professor Brunstein, I think I have finally devised an *ex vivo* culture technique that resolves the inherent limitations of cord blood grafts. I can expand hematopoietic stem cells and stem progenitors by over 10-fold. I can differentiate naïve, pathogen-specific T cells into memory cells that will provide defense against infection early after transplantation. With these methods, I believe we will improve engraftment and reduce non-relapse mortality substantially."

Professor Brunstein:
 "That is wonderful! What will you call this cellular product?"

Assistant:
 "I shall call it"

HLA-haploidentical bone marrow!!!

Question 2: Based upon BMT CTN trials 0603 and 0604, which appear to be true?

1. There is more severe GVHD after cord blood SCT than after haploBMT
2. Relapse is worse after haplo than after cord SCT
3. Neutrophil recovery is faster after haplo than after cord blood SCT
4. Event-free survival is better after haplo than cord

A. 1, 2, and 3
 B. 1 and 3
 C. 2 and 4
 D. 4 only
 E. All of the above
