

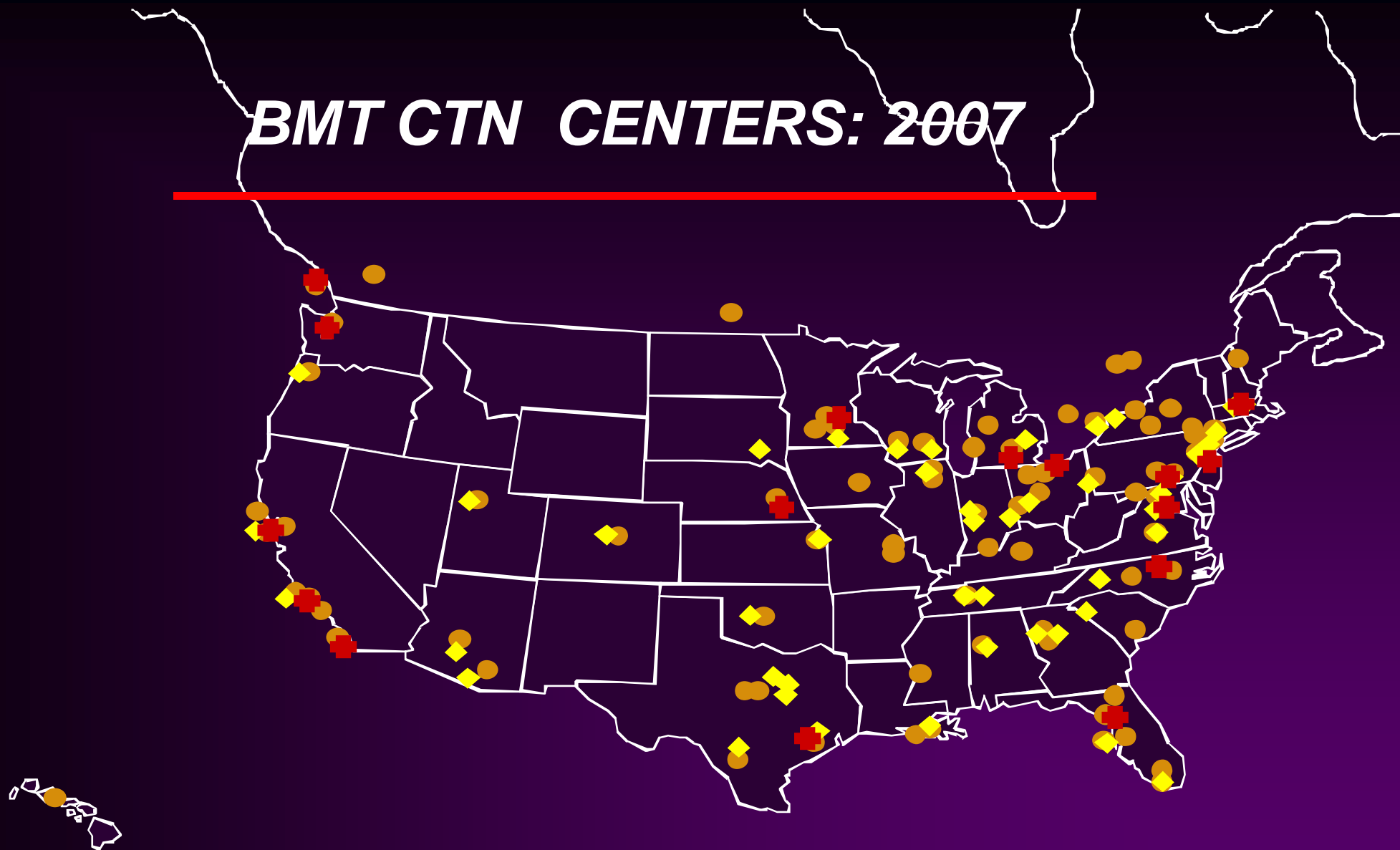





Research Agenda in Myeloma

BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

- ***Established in November 2001***
- ***Mission: Conduct scientifically meritorious multicenter trials in an efficient manner to improve transplant outcomes***
- ***Provide the infrastructure to allow promising therapies to be developed/evaluated in high quality multicenter studies that give definitive answers as rapidly as possible***

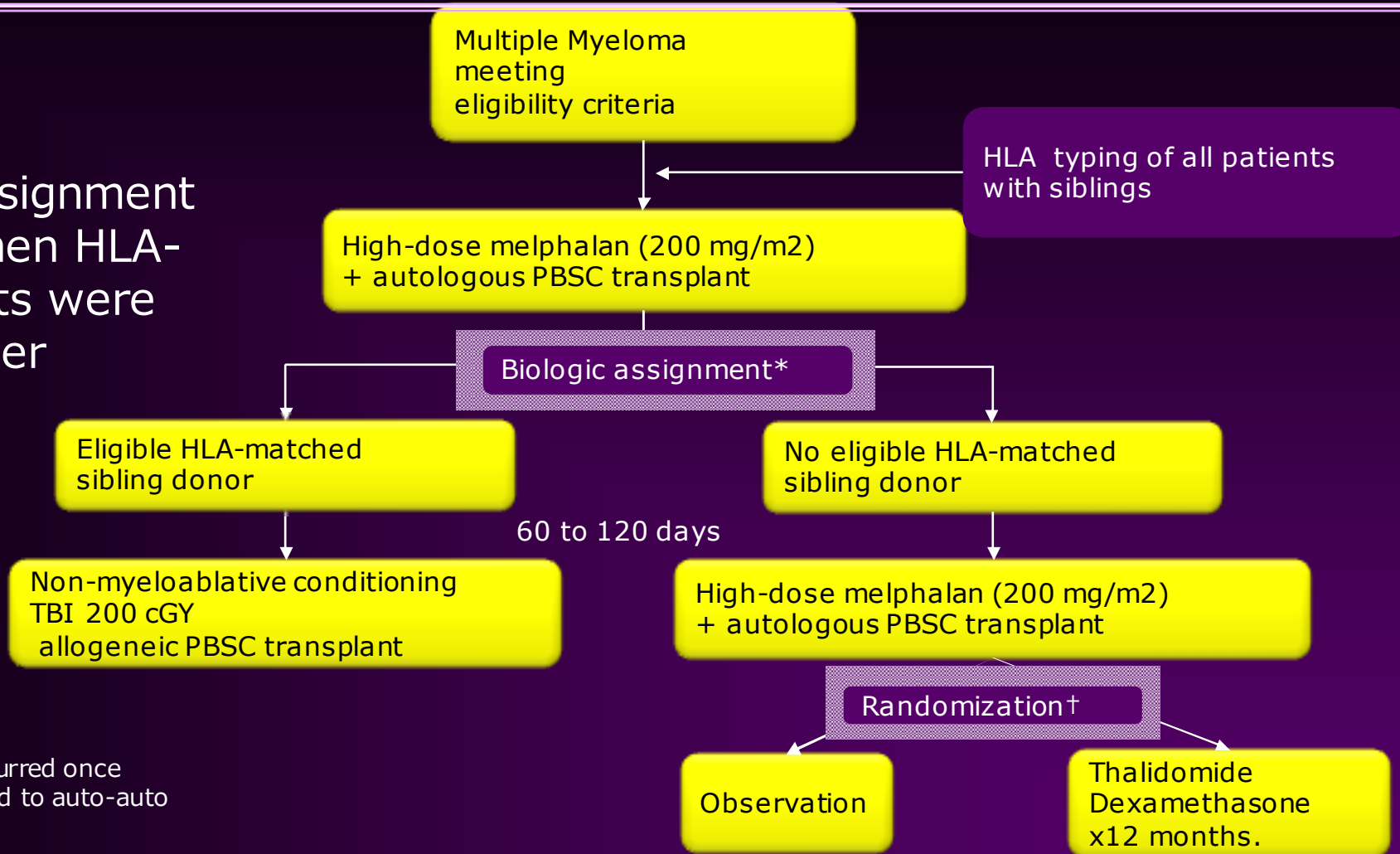
BMT CTN CENTERS: 2007



-  = Core Centers
-  = Other Centers
-  = PBMTC Centers

BMT CTN 0102 Study Schema

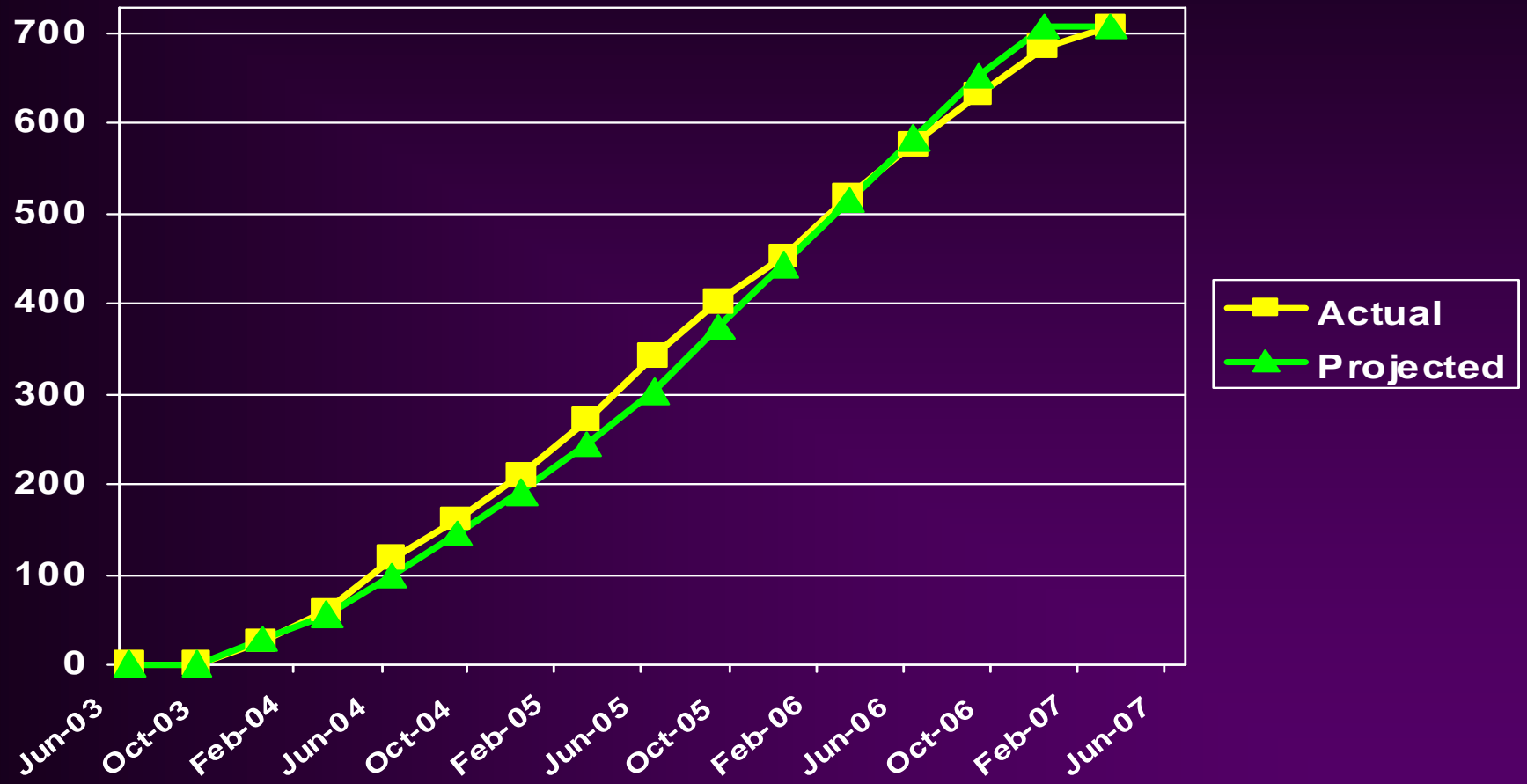
*Biologic assignment occurred when HLA-typing results were available after enrollment.



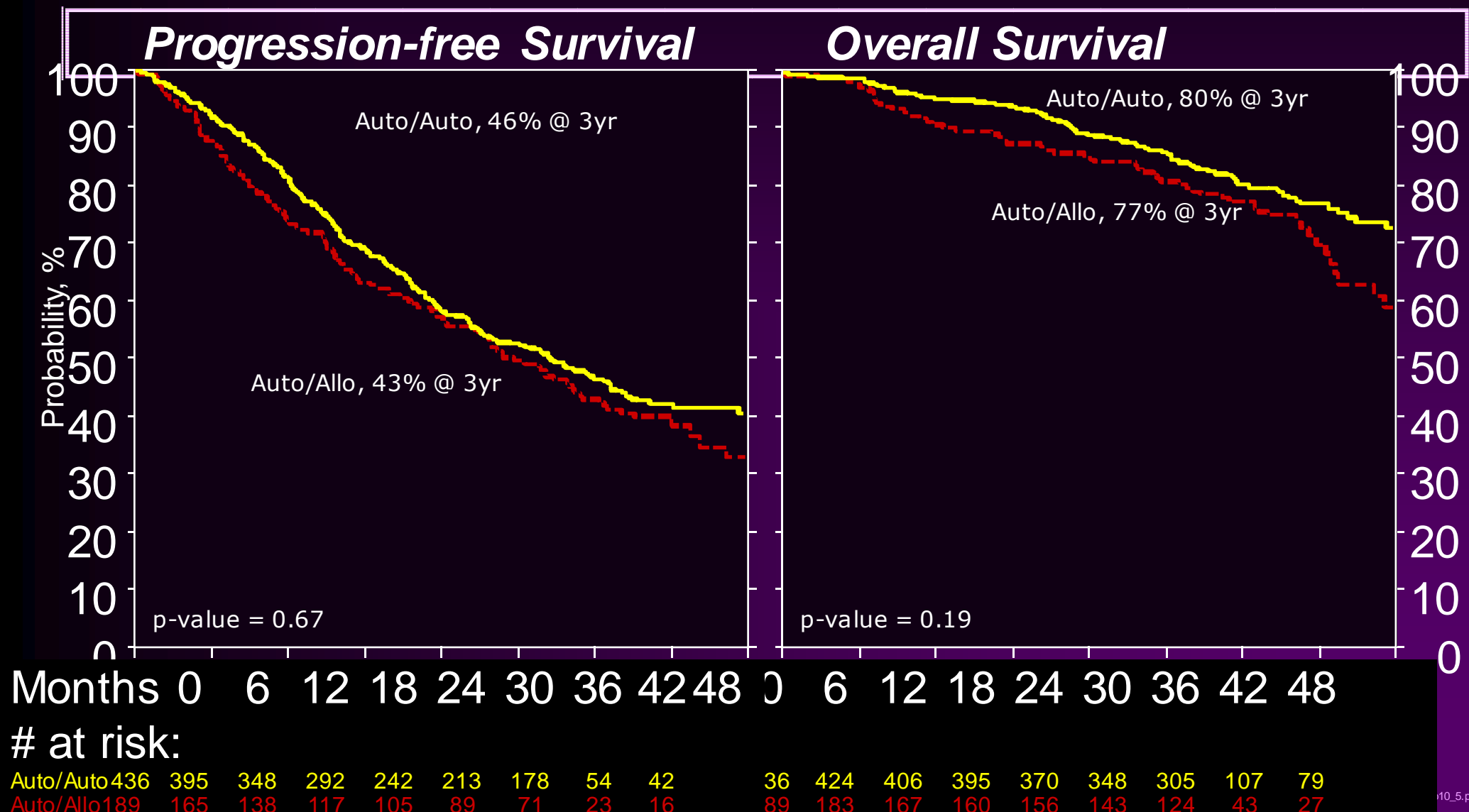
† Randomization occurred once patients were assigned to auto-auto

PRIMARY ENDPOINT : 3yr Progression Free Survival

Accrual to 0102



Survival Outcomes after the First Transplant: Auto-Auto vs. Auto-Allo: Intent-to-treat analysis



Correlatives and Future Proposals

- *Free and Heavy Lite Chain Assays as predictor of outcomes*
 - *H.Parimasweran and M.Pasquini*
- *Meta-analysis Auto-Allo*
 - *D.Vesole-B. Bruno-J.Koreth*
- *4,14 PCR*
 - *R.Fonseca*

***Intergroup Conference on Hematopoietic
Stem Cell Transplantation in Multiple
Myeloma***

***CTN Myeloma Committee
Face to Face Meeting
October 2006***

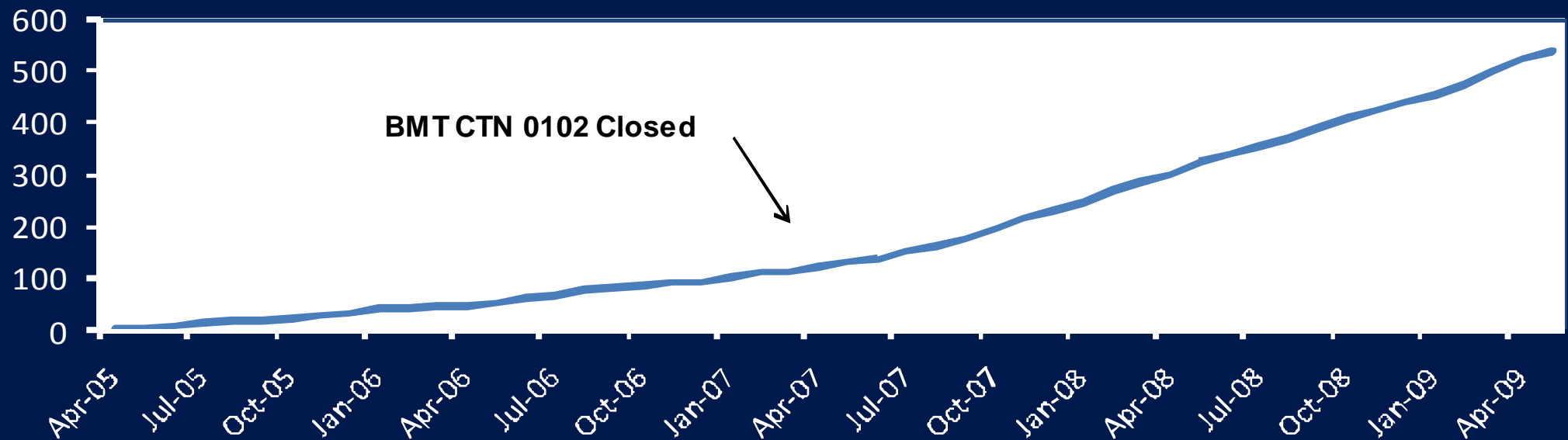
CALGB 100104

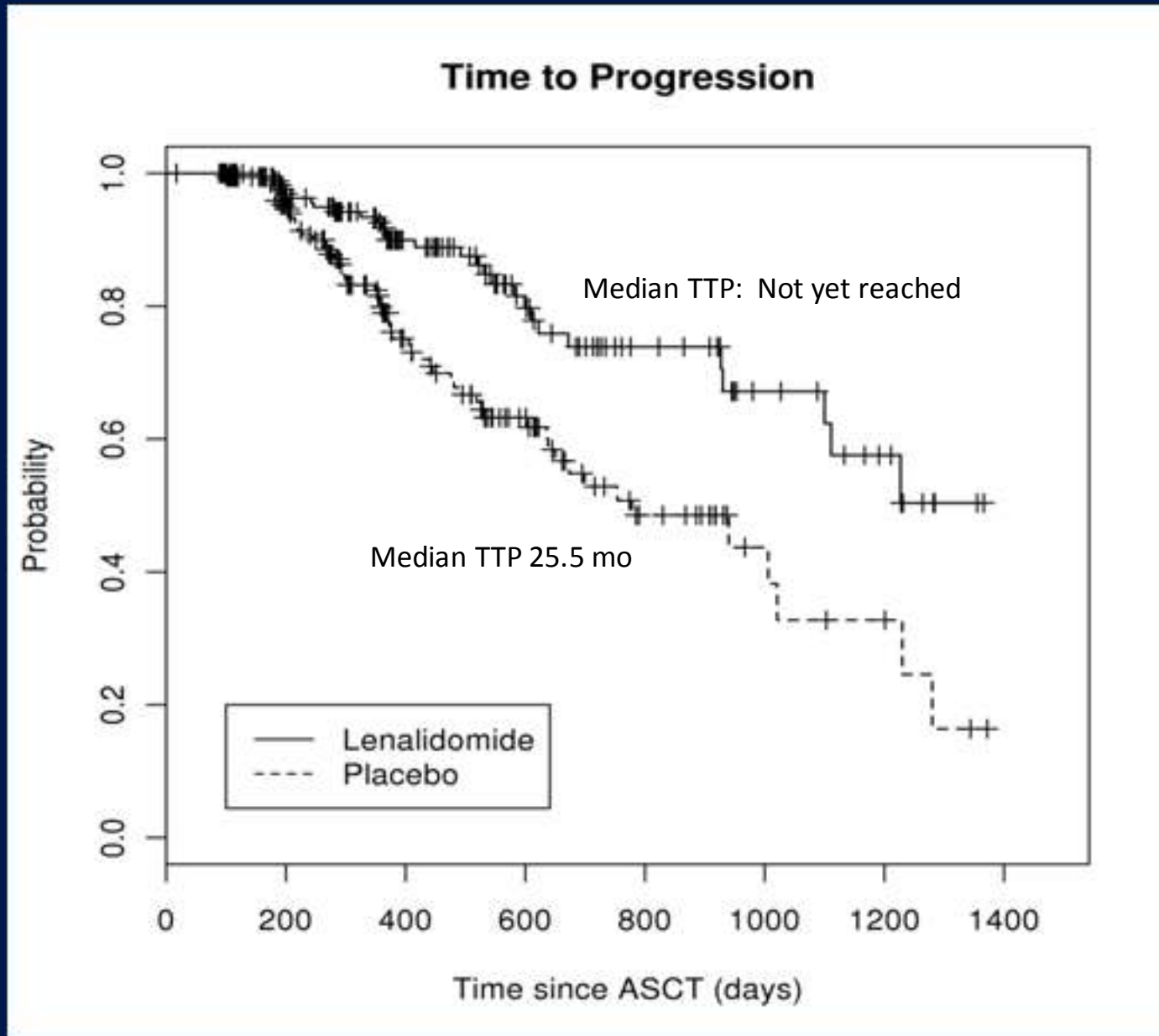
A Phase III Randomized, Double-Blind Study of Maintenance Therapy With Lenalidomide (CC 5013) or Placebo Following Autologous Stem Cell Transplantation for Multiple Myeloma



Philip McCarthy, Roswell Park Cancer Institute, representing CALGB, ECOG and BMT CTN

Monthly Accrual

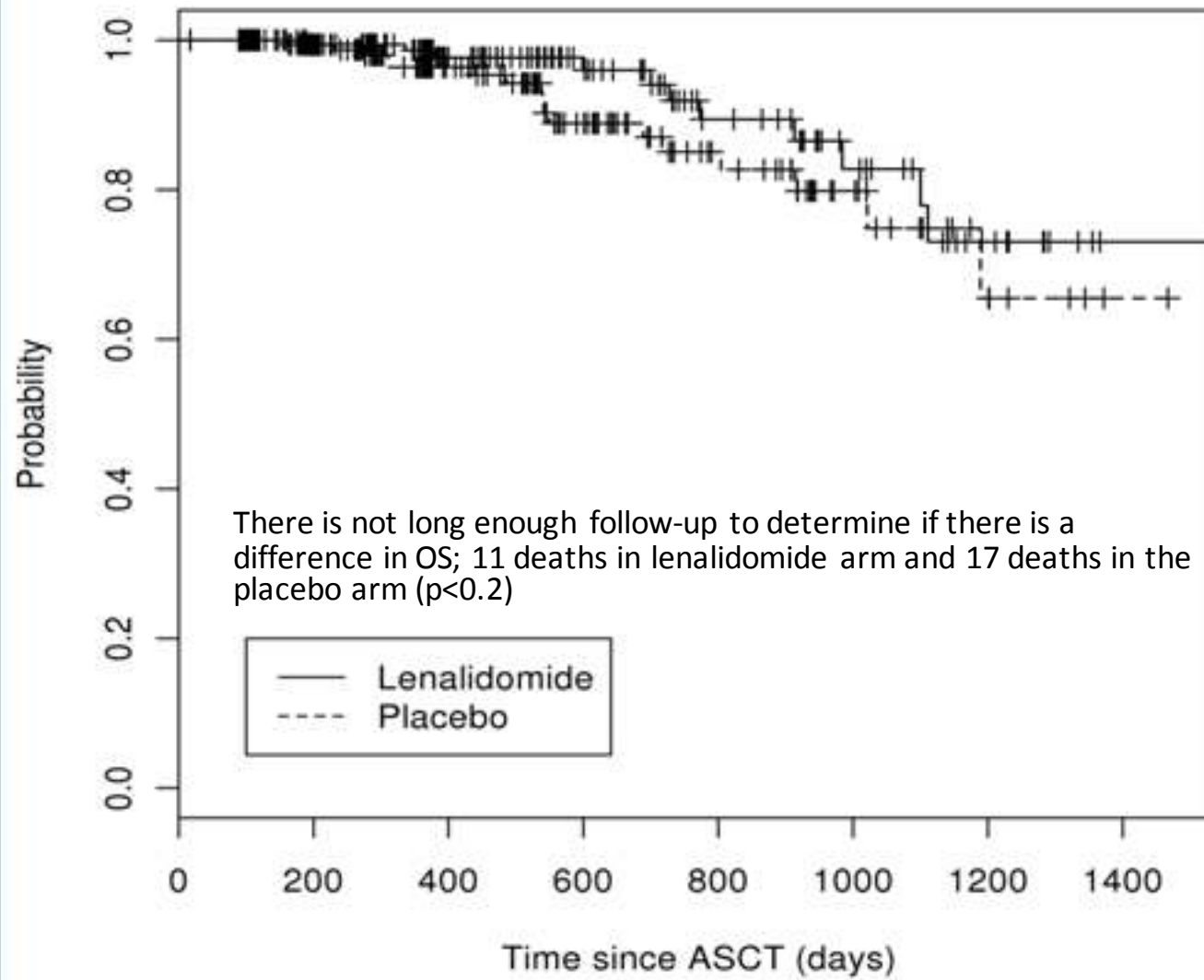




CALGB 100104, Nov 2009

Median Follow up from ASCT is 12 months

Overall Survival



Future Proposals

- Combine datasets with IFM05 to develop risk factors for second primary malignancies
- Case controls against bortezomib maintenance trials



State of the Science Symposium

Myeloma Sub-committee

**Kenneth Anderson, Bart Barlogie, Ray Comenzo,
Sergio Giralt, Jean Luc Harousseau, Nikhil
Munshi, Vince Rajkumar, Keith Stewart, David
Vesole, Robert Vescio**

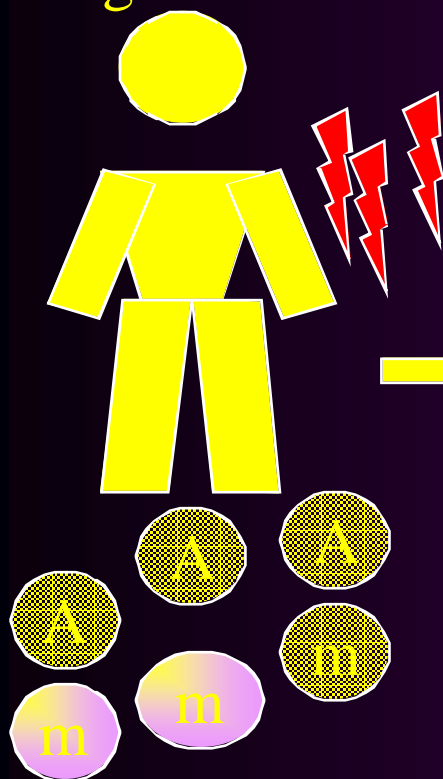
***The Most Compelling
Questions in Myeloma***

Initial Survey From The Committee

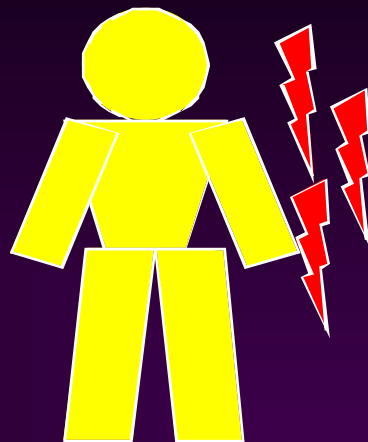
	1	2	3	4	5	6	7	8	9
Novel therapies pre/ post auto HCT	x	X			X	X	X		
Role of Allografting Augmenting GVM	X		X <i>Bort</i>			X	X	X	
Role of upfront autografting	X				X	X		x	
Value of CR after non transplant Tx		X		X	X				
Risk profiling with gene arrays		X		X			X		
Improving prep regimen			X						X <i>Len</i>
Consolidation Maintenance			X					x	X
Reducing toxicities									X
Salvage therapies				X					

EARLY VS LATE HCT: should we try again?

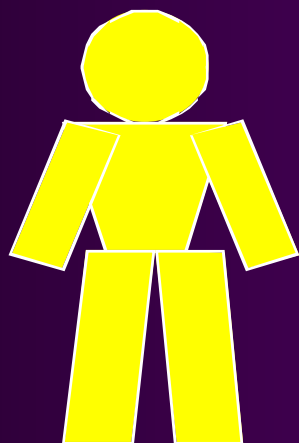
Optimal
Induction
Regimen



Risk Profile

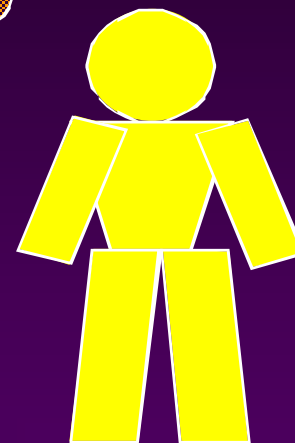
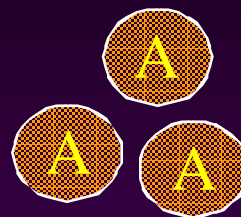


or



COLLECT graft

Auto HCT



Maintenance



HARVEST and HOLD

HCT at RELAPSE

EARLY VS LATE HCT STUDY

PROS

- *previous randomized trials dated.*
- *Spare patients high dose therapy*
- *Validate surrogate endpoints for PFS*
- *Important question for patients.*

CONS

- *Optimal induction therapy unknown.*
- *Optimal maintenance therapy unknown*
- *Potential for bias*
- *No equipoise*
- *Large numbers or long accrual times.*
- *Not applicable for patients referred for HCT*

Hypothesis

***Incorporation of new agents as post
transplant consolidation will improve EFS
compared to
consolidation with second autologous HCT.***

BMT CTN 0702

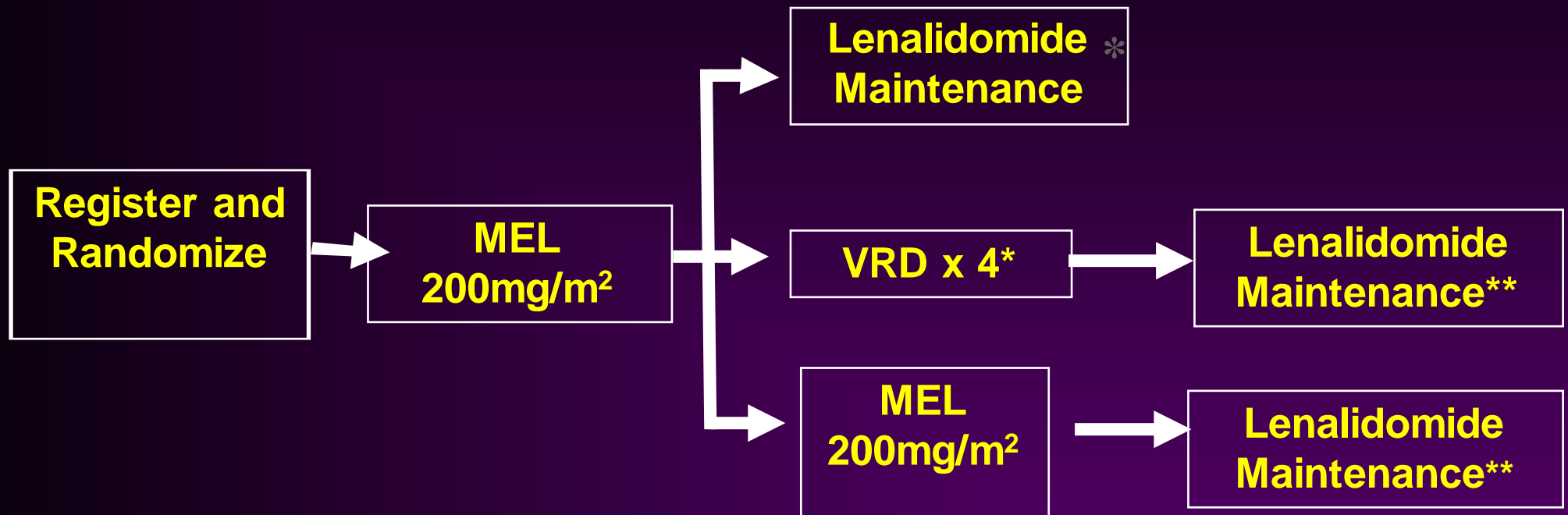
*A Trial of
or without
Transp*

*plant with
is Tandem
erapy.*



Stem Cell Transplantation for
Multiple Myeloma Incorporating Novel Agents

BMT CTN 0702: SCHEMA



* Bortezomib 1.3mg /m² days 1, 4, 8, 11
Lenalidomide 15mg days 1-15
Dexamethasone 40mg days 1, 8, 15

**Lenalidomide 15 mg daily x 3years



Statistical Considerations

- ***Primary Objective: EFS at 3 years (60% vs 45%)***
- ***Sample size: 225 pts per arm
(675 total, similar to BMT CTN 0102)***
- ***Compare single transplant vs. consolidation vs. tandem transplant plus maintenance***
- ***80% power to detect differences in EFS $p=0.025$***
- ***Correlatives***
 - ***MRD by Flow***



August 08 Steering Committee decides whether to distribute this protocol to non CALGB100104 centers. PROTOCOL NOT OPEN TO ACCRUAL UNTIL Q2 2010.

An elephant is born

Animal Average gestation period (days)

Rabbits	30
Cats	62
Dogs	65
Lions	110
Pigs	115
Sheep	150
Humans	259-294
Cattle	283
Elephants	600-660
CTN0702	532 days

Prediction is a hazardous business...



***"Airplanes have no
military value."
- Marshal Foch***



***"640,000 bytes of
memory ought
to be enough for
anybody."
- Bill Gates, 1981***