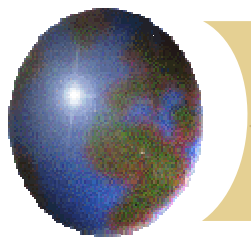


# International Myeloma Working Group Consensus Statement

## Second Primary Cancers

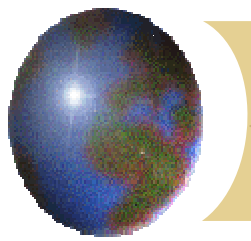
**January 30-31, 2011  
Santa Monica, CA**





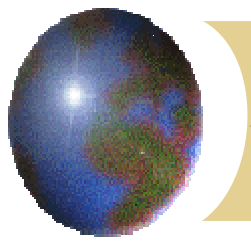
# IMWG - Consensus Statement

- ❖ The occurrence of second cancers in patients with MM has been recognized for decades. The risk of AML/MDS is increased and is related to melphalan based therapy. For solid tumors, the occurrence is similar to that expected in an age matched population.
- ❖ Several randomized trials show that treatment with lenalidomide significantly reduces the risk of progression in relapsed MM and when used as maintenance therapy. At this point, overall survival improvement has been noted in relapsed MM trials, and no improvement in overall survival has been noted in maintenance trials.



# IMWG - Consensus Statement

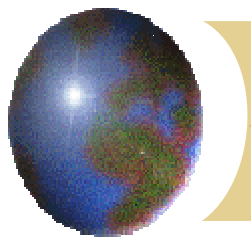
- ❖ Three large studies presented at ASH 2010 raised questions about the occurrence of second primary cancers in the setting of lenalidomide use.
- ❖ An increase in the number of second cancers was reported in 2 trials (CALGB & IFM: see table) in which lenalidomide was administered as maintenance after high dose melphalan based stem cell transplantation.
- ❖ In the third trial, in the frontline setting (MM015: see table), an increase in the number of second cancers was reported with the use of lenalidomide in combination with melphalan. Separately, in a SWOG trial (0232), which used lenalidomide without melphalan no increased risk has been reported.
- ❖ Because of the potential for increased risk of second cancers some investigators have decided to limit the duration of lenalidomide maintenance.



# Second Primary Cancers\*

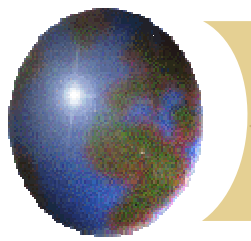
IFM			
	Len	17/299	5.5%
	Placebo	3/292	1.0%
CALGB			
	Len	15/231	6.5%
	Placebo	6/229	2.6%
MM015			
	MPR	11/355	3.1%
	Placebo	2/154	1.3%

\*Numbers and % as of 2/6/11  
Basal cell cancers excluded



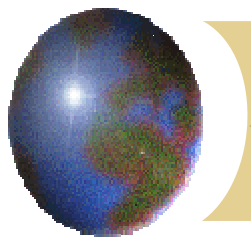
# IMWG - Consensus Statement

- ❖ At this time, no increased incidence of second cancers has been reported with the use of lenalidomide in relapsed refractory myeloma.
- ❖ All trials to date in which an increased number of second cancers occurred, included prior or concomitant melphalan therapy (high or standard dose).



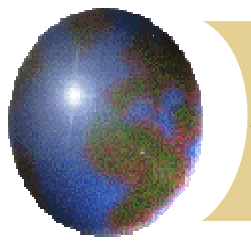
# IMWG - Consensus Statement

- ❖ At the current time the benefits of lenalidomide in relapsed/refractory myeloma are well established.
- ❖ Based on available data IMWG does not recommend changes to currently accepted lenalidomide treatment approaches in the setting of frontline therapy (pre-transplant induction or primary therapy) or in relapsed refractory MM therapy.



# IMWG - Consensus Statement

- ❖ At present, members of the IMWG are split in their opinion concerning the use of lenalidomide as post transplant maintenance. Opinions are strong on both sides of this important issue.
- ❖ A majority feel that the use of lenalidomide should be restricted primarily to clinical trials, and others feel use can be based on clinical judgment.
- ❖ Thus, if post transplant therapy with lenalidomide is used, the IMWG recommends that the potential risk of second cancer be discussed with each patient. The potential for increased risk with longer duration of therapy should also be discussed and considered in making treatment decisions. This treatment decision requires physician/patient discussions to evaluate the benefits of disease control versus potential risks of continued therapy.



# IMWG - Consensus Statement

- ❖ In the clinical trial setting, it is a priority to ensure consistent data collection and reporting of second cancers.
- ❖ It is recommended that information about the potential risk of second cancers be included in the informed consent of experimental trials.

**A concerted effort is underway to further characterize the cases of second cancer that have been reported to define underlying mechanisms and identify risk factors.**