

**To All PRIMA investigators  
Copy for study monitors**

**The PRIMA study reached its goal:  
the DSMC declared the interim analysis POSITIVE,  
Rituximab maintenance after immunochemotherapy  
was found to be significantly superior to observation !**

**Dear Colleague,**

**We would like to share immediately this exciting result!**

The PRIMA independent Data Safety Monitoring Committee (DSMC) met Tuesday September 15<sup>th</sup> to examine the results of the interim analysis. They declared the study positive, meaning that the primary endpoint of the study has been reached at the time of this interim analysis. **This primary endpoint, as described in the protocol, is an increase in progression free survival by 45% in randomized patients.** The DSMC examined the results of the interim analysis with a cut-off date set as January 14<sup>th</sup> 2009. This analysis for the primary endpoint was performed on 1019 randomized patients, with a median follow-up of 24 months. All data obtained before this cut-off date were cleaned and an independent review of CT-scan and response was performed on this population. Investigator assessment of response and independent review of response constituted the basis of the statistical analysis examined by the DSMC. The DSMC recommendation to stop the study was submitted to GELA and Roche senior reviewing members, who decided to follow the recommendation to close the study and examine the full results of the trial. A detailed statistical analysis of the primary and secondary endpoints will be performed in the next few weeks. These results will then be submitted as an abstract to an upcoming scientific meeting. Roche will issue a press release with similar content to the paragraph above.

**We would like to present these results to you exclusively in closed investigator meetings that will be scheduled in Europe and at ASH, before any public communication.**

Meanwhile, please continue to provide follow-up data since an additional update (with a cut-off date of June 30<sup>th</sup>) will be, in addition to the current data, submitted by Roche to the Health Authorities for a rituximab license extension application. Virtually all CRF pages have been collected (thanks again!) and the query process is ongoing, to be completed mid October. The analysis of the study with the final planned 344 events is likely to take place during 2010. **It is therefore important to continue following-up patients until all results become available.** We will update you soon on the upcoming timelines and activities.

**Of note, the DSMC strongly advised not to change the treatment arm already allocated to patients that are still under rituximab maintenance or observation,** given the lack of significant overall survival difference observed. We do support this recommendation, and in any case, any treatment change that you may decide to perform if you think it is in the best interest of the patient should be clearly documented.

**We thank you again for your continuous commitment to the PRIMA study and respecting the timelines for us to obtain this result. This represents an important step forward in the care of follicular lymphoma patients.**

**Again, congratulation to all of you and best regards,**



Professor Gilles Salles