

A multicentre phase III open-label randomized study in patients with advanced follicular lymphoma evaluating the benefit of maintenance therapy with rituximab after induction of response with chemotherapy plus rituximab in comparison with no maintenance therapy.

With the support and effort of all of YOU, we have successfully closed the database for the Interim Analysis.
Thanks from the PRIMA Study Management Team!

Topics

- Database closure for Interim Analysis.
- Next Steps.
- Timelines:
 - DSMC
 - Filing Snapshot

Database Closure for Interim Analysis

We have successfully closed the database for Interim Analysis. Moreover, the independent review of CT-scans by BioClinica (formerly Bio-Imaging) has been achieved in due time. It has been hard work for all of us, but with your support and collaboration we have achieved this important milestone.

Thanks!

Next Steps

As mentioned before, we have met an important milestone for the Interim Analysis. Please be reminded that:

- **The PRIMA Study is still ongoing and patients continue to be treated and followed-up as per protocol.**
- The monitoring frequency will not change. The CRAs will inform you of any details related to monitoring frequency.
- The data from the Interim Analysis will be evaluated by the DSMC in September (see corresponding box below for further information).
- Depending on the feedback received from the DSMC, the trial could be filed in 2010, or we will continue until we reach 344 PFS Events needed for the Final Analysis (see below).
- **It is important to continue reporting PFS events per FAX to GELARC, immediately after they have been detected, as well as collecting all available clinical and safety data on an ongoing basis.**
- CT scan collection with BioClinica will be continued until further notice.

Timelines

The **DSMC** will meet on September, 15th 2009 in order to evaluate and discuss the data at the time of the Interim Analysis (cut-off date: January 14th 2009). Based on the feedback received from the DSMC, there are two most probable scenarios for the future of PRIMA:

1. The DSMC considers the data not mature enough: The study continues as it is right now, and we wait until we have 344 PFS events reported, in order to run the Final Analysis as per protocol.
2. The DSMC considers the data mature enough and positive: The study would be submitted for presentation at an upcoming Scientific Meeting and Roche will file an application in 2010.
 - An updated data set (Filing Snapshot) will be needed for the filing, as the cut-off date for the Interim Analysis was in January 2009.
 - The Clinical cut-off date for the Filing Snapshot has been set as 30-JUN-2009 (see timelines and details in the next box).
 - We expect a considerable number of events and follow-up data to be available since the Interim Analysis and this update will need to be cleaned.

Even though the Filing Snapshot would only apply if we proceed with submission based on Interim Analysis data, we aim to be ready and work pro-actively to achieve this goal if needed. Therefore, several tasks will have to be performed in the near future. The timelines for this snapshot are as follows:

- Clinical Cut-off date: 30-JUN-2009
- Last CRF Page at GELARC: 03-SEP-2009
- Last Query resolved by FAX: 09-OCT-2009
- Last Re-Query resolved by FAX: 16-OCT-2009
- Roche/GELARC review of any last outstanding discrepancies: 19-OCT-2009
- Last Query sent/resolved by FAX for any discrepancy detected above: 20-OCT-2009
- Clean Database Transfer: 21-OCT-2009 (this activity must be started in the evening of 20-OCT-2009)

Adverse Events Reporting

Real time reporting of Adverse Events (AE) is required in this study as data are reviewed on an ongoing basis by our Data Safety Monitoring Committee (DSMC).

Please do not delay reporting of AEs, even incomplete CRF AE pages (e.g. missing end date) are processed and follow up information can then be reported on the **Complementary Information of Adverse Event** CRF page (pages 58-61).

PLEASE REMEMBER

1. During Maintenance period with or without Rituximab, patients must have clinical visits every 8 weeks. It is critical to maintain this evaluation as planned in the protocol to avoid any biases between the 2 arms. Refer also to DSMC feedback letter distributed early last year.
2. After 24 months maintenance period the Evaluation at the End of Treatment forms (CRF pages 34, 35, 36) need to be completed independently of how many visits have been done.
3. If a patient is withdrawn due to Treatment Toxicity (AE or SAE reporting action taken with study drug as *discontinued*) the withdrawal page needs to be completed as soon as possible, with reason due to toxicity.

IN CASE OF QUESTIONS**Medical questions: please contact**

- Prof. Gilles Salles at GELA
(gilles.salles@chu-lyon.fr)
- Denitza Muller at GELARC
(denitza.muller@gelarc.org or
+33 4 72 66 93 33)
- Martin Barrett at Roche
(martin.barrett@roche.com or
+44 1707 36 5943)

Data Management questions: please contact

- Laurence Girard
(laurence.girard@gelarc.org or
+33 4 72 66 93 33)
- Emilie Combalot
(emilie.combalot@gelarc.org or
+33 4 72 66 93 33)
- Denitza Muller or your DM at GELARC

SAE questions: please contact

- Larissa Mege at GELARC
(larissa.mege@gelarc.org)

THANK YOU FOR YOUR CONTINUOUS SUPPORT AND COMMITMENT!