

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

1012 out of 1217 registered patients have been randomised as of October 5th, 2007. Only 25 patients to be randomised yet.

Status: 1217 patients registered

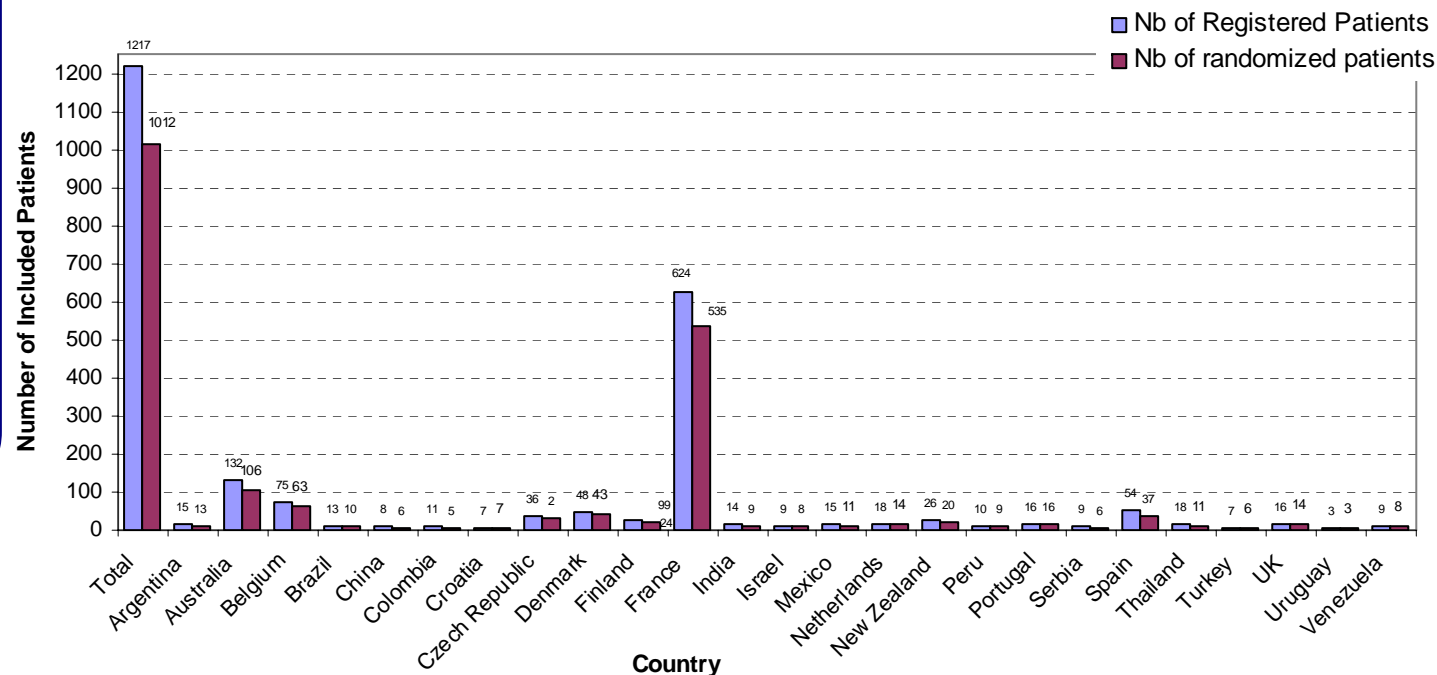
Induction treatment allocation:

- R-CHOP: 900 patients
- R-CVP: 272 patients
- R-FCM: 45 patients

Randomized: 1012 patients

- Maintenance with Rituximab: 505 patients
- Observation: 507 patients

Country Recruitment - PRIMA study



Timelines 1st Interim Analysis

172 PFS (Progression Free Survival) events are needed to fulfil the protocol requirements for the **First Interim Analysis**.

Upon estimations based on the current PFS event rate in the PRIMA Trial and data from previous similar trials, the **Cut-Off Date** for the analysis is planned by **March 18th, 2008**. This date will be re-evaluated in January 2008 with more updated data on events occurred. All data related to visits performed until this date will be used for the analysis, and must be entered in the database and clean - this means no open discrepancies.

It is planned to lock the database 4 months after the cut-off date. Database lock date is the day by which a snapshot of database is taken for the analysis.

Importance of Immediate Event Reporting

Death or Progression/Relapse pages (pages 47, 47-2, 48 and 49), if applicable to the patient - need to be faxed to GELARC (**FAX +33 4 72 66 93 71**) as soon as the Investigator is informed of the event. These pages must be SDVed and collected during the next monitoring visit.

DSMC Meeting

The PRIMA Data Safety Monitoring Committee will meet on **December 2007** during the ASH Congress. Demographic and Safety data of the PRIMA Trial will be reviewed and evaluated during this meeting. Therefore it is critical that all baseline data and adverse events and toxicity information has been reported on the CRF pages immediately after data are obtained and these data is SDVed and sent to GELARC. CRAs will be willing to provide support and clarify any questions.

An AE page must be completed for each SAE, immediately after faxing the SAE report to the GELA Safety Desk. The CRA will verify the source data and collect this page during the next visit. By SAE form, only one event (=main diagnosis) should be reported. Symptoms should be reported in the narrative. In case of several serious adverse events, one separate SAE form has to be completed for each event.

Monitoring Frequency Will Be Increased

In order to meet the study goals for the First Interim Analysis and the Safety Data Review by the DSMC, it has been decided by the Study Management Team to increase the monitoring frequency to every 4 weeks.

We thank you for your continued support and commitment to the study and we value both your help and time provided to the CRAs in order to achieve our study goals.

CRF RECEPTION STATUS (05/10/2007)

	Patients included	Patients randomized	Baseline Part (p1-9)			p1-2 received (including NA patient)	Induction Part (p10-18)			Nb 10-2, 12-2 complete	Maintenance V1-V4 (p19-23)			Maintenance V5-V8 (p24-28)			Maintenance V9-V12 (p29-33)		
			Complete	Partial	Missing		Complete	Partial	Missing		Complete	Partial	Missing	Complete	Partial	Missing	Complete	Partial	Missing
	%	83,2	98,1	1,4	0,5	69,9	76,6	10,9	12,5	65,0	52,5	33,0	34,8	25,0	24,7	70,6	16,5	8,5	95,3
TOTAL	1217	1012	1194	17	6	851	932	133	152	791	531	334	352	253	250	714	167	86	964
Argentina	15	13	15	0	0	0	15	0	0	0	6	7	2	1	8	6	1	0	14
Australia	132	106	126	2	4	63	85	8	39	41	36	41	55	14	20	98	11	3	118
Belgium	75	63	74	1	0	65	66	4	5	69	49	16	10	32	17	26	17	14	44
Brazil	13	10	12	1	0	12	7	0	6	6	3	2	8	0	2	11	0	0	13
China	8	6	8	0	0	8	2	3	3	5	1	1	6	0	1	7	0	0	8
Colombia	11	5	11	0	0	7	8	3	0	10	2	2	7	1	0	10	0	1	10
Croatia	7	7	7	0	0	4	7	0	0	1	7	0	0	0	4	3	0	0	7
Czech Republic	36	30	36	0	0	24	34	2	0	21	23	10	3	1	16	19	0	1	35
Denmark	48	43	48	0	0	47	44	2	2	45	30	12	6	13	16	19	6	6	36
Finland	24	22	24	0	0	24	19	2	3	21	6	11	7	2	4	18	2	0	22
France	624	535	617	6	1	435	473	83	68	444	274	179	171	148	119	357	96	57	471
India	14	9	14	0	0	3	14	0	0	0	12	2	0	7	5	2	6	0	8
Israel	9	8	9	0	0	9	4	4	1	7	0	4	5	0	0	9	0	0	9
Mexico	15	11	15	0	0	0	15	0	0	0	6	6	3	2	4	9	2	0	13
Netherlands	18	14	14	4	0	10	16	1	1	10	1	10	7	1	0	17	1	0	17
New Zealand	26	20	25	0	1	22	15	1	10	14	9	5	12	1	6	19	1	0	25
Peru	10	9	10	0	0	0	2	6	2	1	3	3	4	2	1	7	2	0	8
Portugal	16	16	16	0	0	15	16	0	0	5	1	1	14	0	0	16	0	0	16
Serbia	9	6	9	0	0	2	7	0	2	0	0	3	6	0	0	9	0	0	9
Spain	54	37	54	0	0	51	42	11	1	51	37	4	13	19	12	23	16	2	36
Thailand	18	11	18	0	0	18	16	0	2	16	13	3	2	8	5	5	5	2	11
Turkey	7	6	7	0	0	6	7	0	0	6	6	1	0	1	4	2	1	0	6
UK	16	14	13	3	0	14	7	3	6	7	0	7	9	0	0	16	0	0	16
Uruguay	3	3	3	0	0	3	2	0	1	2	0	2	1	0	0	3	0	0	3
Venezuela	9	8	9	0	0	9	9	0	0	9	6	2	1	0	6	3	0	0	9

CT Scan Collection Update by Bio-Imaging

- ✓ The CT Data Collection for the GELA PRIMA study is well under way! Bio-Imaging is asking you for your continued assistance as we continue our efforts towards collecting all available CT data.
- ✓ Please remember that Bio-Imaging will only be collecting the CT/MRI scans of randomized patients that have approved protocol amendment 3 and signed ICF versions 2.0/2.1. If you cannot locate a patient on this spreadsheet it is likely because we are not able to collect the data yet.
- ✓ Our team at Bio-Imaging is here to assist you with the data collection. Please let me know how we can assist and we will ensure that your needs are met.

FAQ:

- Q: What type of digital data is acceptable at Bio-Imaging?
A: Any digital data should be submitted in uncompressed DICOM format. This is the most widely used format of imaging data.
- Q: I am in need of additional supplies. What do I need to do?
A: In the event that you require additional supplies, please email supplies@bioimaging.com or contact the Project Management team at Bio-Imaging (rcella@bioimaging.com, mvdkooi@bioimaging.com, or rvincenten@bioimaging.com).
- Q: I have collected the patient data from my site. Now what?
A: Firstly, please ensure that the data is from a randomized patient that has signed ICF versions 2.0/2.1 and the site has approved protocol amendment 3. After this is confirmed, the data should be labeled using the protocol specific labels that are found in the Imaging Study Kit. A retrospective Data Transmittal Form (rDTF) should be prepared and submitted to Bio-Imaging. Please remember, one DTF per each patient timepoint.

Questions or concerns: Please contact Ryan Cella (rcella@bioimaging.com), Marieke van der Kooi (mvdkooi@bioimaging.com), Rianne Vincenten (rvincenten@bioimaging.com), and/or Karen Kubacke (kkubacke@bioimaging.com).

Assessment of Haematological Lab Value

If hematological toxicity Grade 3 and 4 is reported for Hemoglobin, Leukocytes, Neutrophils and Platelets, please find an extract of the CTCAE v.3 below, where you can easily verify CTC grade lab value to be reported on the toxicity page.

BLOOD/BONE MARROW						
		Grade				
AE	Short name	1	2	3	4	5
Hemoglobin	Hemoglobin	<LLN – 10.0 g/dL <LLN – 6.2 mmol/L <LLN – 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80 – 65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Leukocytes (total WBC)	Leukocytes	<LLN – 3000/mm ³ <LLN – 3.0 x 10 ⁹ /L	<3000 – 2000/mm ³ <3.0 – 2.0 x 10 ⁹ /L	<2000 – 1000/mm ³ <2.0 – 1.0 x 10 ⁹ /L	<1000/mm ³ <1.0 x 10 ⁹ /L	Death
Neutrophils/granulocytes (ANC/AGC)	Neutrophils	<LLN – 1500/mm ³ <LLN – 1.5 x 10 ⁹ /L	<1500 – 1000/mm ³ <1.5 – 1.0 x 10 ⁹ /L	<1000 – 500/mm ³ <1.0 – 0.5 x 10 ⁹ /L	<500/mm ³ <0.5 x 10 ⁹ /L	Death
Platelets	Platelets	<LLN – 75,000/mm ³ <LLN – 75.0 x 10 ⁹ /L	<75,000 – 50,000/mm ³ <75.0 – 50.0 x 10 ⁹ /L	<50,000 – 25,000/mm ³ <50.0 – 25.0 x 10 ⁹ /L	<25,000/mm ³ <25.0 x 10 ⁹ /L	Death

Please also refer to <http://ctep.cancer.gov/forms/CTCAEv3.pdf>

PLEASE REMEMBER

- ✓ During Maintenance period with or without rituximab, patient 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.
The whole Maintenance period should not exceed two years in total.
- ✓ It is important to follow the target lesions identified at baseline and all through the study, especially if they don't disappear. Usual nodal lesions should be identified by 2 dimensional measurements, using the same imaging technique.
- ✓ A few women in age of procreating became pregnant during the rituximab maintenance period and had therefore to interrupt their treatment. Please strongly recommend a contraceptive measure during this period for the relevant patients.

THANK YOU FOR YOUR CONTINUOUS SUPPORT AND COMMITMENT

If you have any questions or comments about any aspect of the study, please contact your CRA, your Country Study Contact or GELARC.