2. STUDY SYNOPSIS

Name of Sponsor/Company: Biogen Idec Inc./Biogen Idec Ltd.	**Individual Study Table Referring to Part <> of the Dossier** **Volume:** **Page:**	***(For National Authority Use only)***
Name of Finished Product: Lumiliximab (IDEC-152)	**Name of Active Ingredient:** Lumiliximab (IDEC-152)	**Study Indication:** Chronic lymphocytic leukemia

Title of Study:

A Phase 2, Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Fludarabine, Cyclophosphamide, and Rituximab (FCR) in Combination with Lumiliximab Versus FCR Alone in Subjects with Previously Untreated Chronic Lymphocytic Leukemia

Study Period:	**Phase of Development: 2**
Date of first treatment: 23 March 2009 Date of early study termination: 18 February 2010 Last subject last visit: 31 March 2010	

Study Objectives:

Study 152CL202 (LIFT) was originally designed to evaluate whether lumiliximab when combined with fludarabine, cyclophosphamide, and rituximab (FCR) versus FCR affects electrocardiogram (ECG) results, with focus on the QT interval corrected by Fridericia method (QTcF) in subjects with previously untreated CLL and to evaluate the effect of lumiliximab on the pharmacokinetics of fludarabine, cyclophosphamide, and rituximab in subjects with previously untreated CLL.

LIFT was a supportive study to enable a registration filing which was based on a pivotal Phase 2/3 study (LUCID). At the first interim analysis of LUCID it was found that LUCID was underpowered for the end of Phase 2 endpoint of complete response (CR) rate; therefore, recruitment into the LUCID study was stopped and it was converted to a non-registrational Phase 2 study. As LIFT was no longer required as a supportive study for registration, recruitment into LIFT was also stopped, and the primary objective of LIFT was amended to only evaluate the safety and tolerability of subjects still undergoing treatment. Results of the second interim analysis of the LUCID study did not show an efficacy advantage for lumiliximab in combination with FCR and both the LIFT and LUCID studies were terminated early. The planned lumiliximab development program in CLL was stopped.

Primary objective:

- To evaluate the safety and tolerability of FCR in combination with lumiliximab (FCR+L) compared with FCR alone in subjects with previously untreated CLL.

Secondary objective:

- To evaluate the efficacy of FCR+L compared with FCR alone in subjects with previously untreated CLL.

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Study Design:

Study 152CL202 (LIFT) was a Phase 2, randomized, open-label, multicenter study in subjects with previously untreated chronic lymphocytic leukemia (CLL).

Approximately 40 subjects were to be randomly assigned in a 1:1 ratio to 1 of 2 treatment groups through a central randomization process. Approximately 20 sites worldwide were to participate in this study.

The study period for each subject was to be approximately 37 weeks (a screening period up to 1 month followed by a treatment period up to 6 months, then 2 months of follow-up). The study treatment was to be delivered over six 28-day cycles. Cycle 1 was to include 3 days of fludarabine and cyclophosphamide plus 1 stepped-up dose of either rituximab and lumiliximab (Treatment Group A) or rituximab (Treatment Group B). Cycles 2 to 6 were to include 3 days of fludarabine and cyclophosphamide plus either rituximab and lumiliximab (Treatment Group A) or rituximab (Treatment Group B).

Subjects were to complete scheduled visits until Week 33. Subjects who had already completed visits past Week 33 at the time of implementation of Protocol Version 3 were to be asked to return for a final Study Completion Visit.

LIFT was terminated early when the results of the pivotal study (LUCID) indicated that there was not sufficient efficacy with the addition of lumiliximab to FCR to continue clinical development of lumiliximab in CLL.

Number of Subjects (Planned and Analyzed):

Approximately 60 subjects (30 per treatment group) were planned originally; however, this was changed to approximately 40 subjects in Version 3; and 40 subjects were analyzed.

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Results:

Subject disposition:

Forty subjects were randomized and were dosed in this study: 20 subjects received FCR+L and 20 subjects received FCR only. Thirty-six of the 40 subjects (90%) completed the study. Four subjects withdrew from the study for the following reasons: adverse event (2 subjects in the FCR treatment group), personal reasons (1 subject in the FCR+L treatment group), and withdrew consent (1 subject in the FCR+L treatment group).

Demographics and baseline disease characteristics:

Demographics were similar for both treatment groups. Most subjects were white (98%) and male (70%), and they ranged in age from 31 to 80 years of age. Most baseline disease characteristics were similar; however, of interest was Rai stage I and II at study entry. Rai stage was I for 11 (55%) subjects in the FCR+L treatment group and 4 (20%) subjects in the FCR treatment group and II for 5 (25%) subjects in the FCR+L treatment group and 11 (55%) subjects in the FCR treatment group.

Safety:

- All 40 subjects experienced an adverse event (AE).
- The severity of AEs was similar between the treatment groups: Grade 1, 2, 3, and 4 events were reported for 1 subject (5%), 8 subjects (40%), 6 subjects (30%), and 5 subjects (25%) in the FCR+L treatment group and 2 subjects (10%), 6 subjects (30%), 9 subjects (45%), and 3 subjects (15%) in the FCR treatment group, respectively. No Grade 5 events were reported.
- Thirty-seven subjects experienced a study-related event: 18 (90%) subjects in the FCR+L treatment group and 19 (95%) subjects in the FCR treatment group. Events occurring in 20% or more of subjects in either treatment group were similar between both treatment groups: nausea (13 [65%] subjects in FCR+L and 10 [50%] subjects in FCR), neutropenia (9 [45%] subjects each in both treatment groups), fatigue (6 [30%] subjects each in both treatment groups), pyrexia (5 [25%) subjects in FCR+L and 6 [30%] subjects in FCR], chills (3 [15%] subjects in FCR+L and 5 [25%] subjects in FCR), decreased appetite (4 [20%] subjects each in both treatment groups), and anemia (2 [10%] subjects with FCR+L and 4 [20%] subjects in FCR).
- Eighteen (90%) subjects had lumiliximab-related AEs. Events reported by more than 1 subject were nausea (9 [45%] subjects); neutropenia (8 [40%] subjects), fatigue (6 [30%] subjects); decreased appetite (4 [20%] subjects); pyrexia (3 [15%] subjects); and asthenia, diarrhea, exertional dyspnea, headache, hypersensitivity, lethargy, leukopenia, rash, rash maculopapular, and vomiting (2 [10%] subjects each).
- No deaths were reported during the study.

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- Five subjects discontinued treatment due to an AE: 3 subjects in the FCR+L treatment group and 2 in the FCR treatment group. One subject discontinued study treatment due to an event of transitional cell carcinoma and another subject due to an event of alcoholism; both of these events were not related to study treatment. Three subjects had events related to lumiliximab: 1 subject had hypersensitivity and allergic edema, 1 subject had neutropenia and leukopenia, and 1 subject had an anaphylactic reaction.
- Thirteen subjects had a serious AE: 6 subjects in the FCR+L treatment group and 7 in the FCR treatment group. Events reported by more than 1 subject in both treatment groups combined were febrile neutropenia (1 subject each in the FCR+L and FCR treatment groups; events were related to study treatment), hypersensitivity (2 subjects in the FCR+L treatment group only; events were related to study treatment), and pyrexia (2 subjects in the FCR+L, events were not related to study treatment; and 1 subject in the FCR treatment groups; event was related to study treatment).
- Two subjects withdrew from the study due to an AE; both were in the FCR treatment group. One subject experienced transitional cell carcinoma beginning on Day 56 and withdrew from the study on Day 256. One subject experienced alcoholism beginning on Day 57 and withdrew from the study on Day 116. Neither of these events were attributed to any component of the study treatment by the Investigator.
- No clinically important differences in the hematology or blood chemistry results were observed between the FCR+L and FCR treatment groups.

Conclusion(s):

- The addition of lumiliximab to FCR was well tolerated and did not appear to add to the toxicity of the FCR regimen.
- There were no unexpected safety findings in this study.
- Biogen Idec has decided not to pursue further development of lumiliximab in CLL.

Date of Report: 04 August 2010