Australian Diabetes Society

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The Peak Medical and Scientific Organisation on Diabetes in Australia

ADS Position Statement on Insulin Glargine (Lantus ®) and a Possible Link with Cancer:
Posted: 15 December, 2009
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Review date: 17 October, 2014 (unless revised or withdrawn earlier)

Summary: New research has provided reassuring data about the safety of insulin glargine.

Introduction:
In June 2009, online publications in the diabetes journal Diabetologia suggested an association between insulin glargine (Lantus ®), and increased risk of cancer. The articles were published in the September 2009 issue. A comprehensive Diabetologia commentary series can be found at http://www.diabetologia-journal.org/.

These population studies collectively included more than 350,000 patients and suggested that there may be a link between glargine (Lantus ®) and cancer risk. Specifically, there was an association between glargine (Lantus ®) when used alone and breast cancer. However, these articles were widely criticised and the statistical methods used were unorthodox.

Subsequent Publications:
An online publication summarising controlled trials in >10,000 patients with type 1 or type 2 diabetes reported no significant difference in the incidence of malignancies, including breast cancer (1). Most of the studies were 6 months or less in duration.

In a 5-year open-label randomised clinical trial in 1017 patients with type 2 diabetes, the overall rate of malignancies was similar in the insulin glargine and NPH groups (insulin glargine 23 (4.5%); NPH 32 (6.4%)) (2). The number of patients with breast cancer was also similar (insulin glargine 3 (0.6%), NPH 4 (0.8%)).

Recently, the results of the ORIGIN (Outcome Reduction with Initial Glargine Intervention) study were published (3). ORIGIN was a randomised, controlled study of >12,500 people assigned to treatment with insulin glargine or placebo. The subjects had an average age of 63 years who had or were at high risk of cardiovascular disease plus (a) impaired fasting glucose, (b) impaired glucose tolerance or (c) type 2 diabetes. For group (c), 8,200 participants had new (760) or previously diagnosed (7,440) type 2 diabetes, with an average duration of diabetes of 5.4 years. Median follow-up was 6.2 years.

Cancer was a pre-specified secondary outcome measure. There was no increase in risk of any cancer (Hazard ratio 1.00 (0.88-1.13)), death from cancer (HR 0.94 (0.77-1.15)) or death from any cause (HR 0.98 (0.90-1.08)).The risk for individual cancers from the supplemental data are below.

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Site	Hazard Ratio (95% CI)	p-value	Total cases
Breast	1.01 (0.60-1.71)	0.95	56
Lung	1.21 (0.87-1.67)	0.27	146
Colon	1.09 (0.79-1.51)	0.61	146
Prostate	0.94 (0.70-1.26)	0.70	177
Melanoma	0.88 (0.44-1.75)	0.71	32
Other	0.95 (0.80-1.14)	0.59	478

The results of the ORIGIN study suggest that there is no increase in risk of cancer in that population, and specifically, there was no increase in the risk of breast cancer.

Each site managed cancer after diagnosis as per their judgment. Clinical course in people who did or did not continue glargine after cancer diagnosis has not been analysed by the ORIGIN investigators. However, ADS notes that there was also no increase in cancer mortality in the study.

Recommendation of the Australian Diabetes Society:

In light of the data from the ORIGIN study and other studies, ADS believes that the current data do not support a relationship between the use of insulin glargine and malignancy. Patients with diabetes taking insulin glargine (Lantus ®) do not need to change their insulin therapy. Patients with diabetes can be initiated on glargine therapy without concern that insulin glargine will increase the risk of developing a malignancy.

However, if after discussion of these facts a patient still has ongoing concerns; it would be prudent to consider advising alternate treatment.

Potential conflict of interest statements relevant to insulin glargine (Lantus ®):

- ADS receive support for the ADS Annual Scientific Meeting from Sanofi-Aventis as a principal sponsor and have standard commercial arrangements for Sanofi-Aventis to display at the ADS Annual Scientific Meeting.
- Michael D'Emden and Ashim Sinha have received honoraria, travel support and/or payment for participation in Sanofi-Aventis advisory committees.

References:

1) Home PD and Lagarenne P. (2009) Combined randomised controlled trial experience of malignancies in studies using insulin glargine. Diabetologia. http://www.springerlink.com/content/r644844411g51752/fulltext.html
2) Rosenstock J et al. (2009) Similar risk of malignancy with insulin glargine and neutral protamine Hagedorn (NPH) insulin in patients with type 2 diabetes: findings from a 5 year randomised, open-label study. Diabetologia. http://www.springerlink.com/content/131t04q531710g21/fulltext.html
3) ORIGIN Trial Investigators. (2012) Basal Insulin and Cardiovascular and Other Outcomes in Dysglycemia. *New England Journal of Medicine*, DOI 10.1056/NEJMoa1203858.

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