

July 10, 2009

Does insulin glargine (Lantus<sup>®</sup>) cause CANCER?**Bottom Line**

**The evidence presented below is sufficient to establish some significant concerns about insulin analogues and cancer risk, but is completely insufficient to bring in a verdict.**

**What happened yesterday?**

- Health Canada began performing a safety review for a possible link between insulin glargine (Lantus<sup>®</sup>) and cancer (as did their U.S. and EU counterparts)

**What is Insulin Glargine?**

- It is a long acting synthetic insulin analogue
- **Insulin detemir (Levemir<sup>®</sup>)** is the other long acting insulin analogue available in Canada.
- Insulin analogues are **not more effective than human insulins (e.g., Humulin N)**, but they carry a somewhat lower risk of nocturnal hypoglycemia

**What did we know about insulin and cancer before today?**

- It is well known that diabetes is a risk factor for cancer
- ↑ cancer in diabetes is thought to be linked with high circulating levels of insulin
- Insulin has been shown to have mitogenic effects & observational studies have made possible links between ↑ cancer risk with human insulin use OR drugs that ↑ insulin levels (sulfonylureas).

**How might analogues (like glargine) cause MORE cancer?**

- This is not known...BUT it is possible that synthetic changes to the molecular structure of human insulin MAY change the mitogenic effects (leading to more cancer)
- Previous in-vitro studies suggest that insulin analogues may promote the growth of cancer cells (in a Petri dish) MORE than human insulins

**What is the NEW evidence?**

- Four separate studies were published this month
- All are retrospective, observational studies using health databases in Germany, Sweden, Scotland and UK.
- The studies compared the use of insulin glargine and human insulins with cancer diagnoses.
- **The other long acting insulin analogue (insulin detemir) was NOT studied as it was not available at the time.**

**Link to Health Canada safety report**

[http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2009/2009\\_115-eng.php](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2009/2009_115-eng.php)

**Link to European safety report**

<http://www.diabetologia-journal.org/cancer.html>

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**RxFiles added links:****European – EASD Webcast:**

<http://webcast.easd.org/press/glargine/glargine.htm> ]

**FDA MedWatch:**

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicinalProducts/ucm170089.htm>

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**Link to German study**

[http://www.diabetologia-journal.org/cancer\\_files/081131Hemkenscorrectedproofs.pdf](http://www.diabetologia-journal.org/cancer_files/081131Hemkenscorrectedproofs.pdf)

**Link to Swedish study**

<http://webcast.easd.org/press/glargine/download/090776Jonassoncorrectedproofs.pdf>

**Link to UK study**

<http://webcast.easd.org/press/glargine/download/090740Curriecorrectedproofs.pdf>

**Link to Scottish study**

<http://webcast.easd.org/press/glargine/download/090818Colhoununcorrectedproofs.pdf>

**What did they find?**

- 3 of the 4 studies found higher rates of cancer (overall cancer in the German study, breast cancer in the Swedish study, overall cancer & breast cancer in Scottish study) **after as little as 1.5 years.**

**Can we trust these results?**

- Observational studies are ALWAYS untrustworthy as they can't perfectly match groups at baseline (e.g., **in these studies, groups were not the same for many factors** that could effect cancer rates, such as weight, age, & BP).
- The results have some biological plausibility (breast cancer is thought to be an insulin sensitive cancer) and the consistency of results across 3 studies suggests that this should be taken seriously.
- The fact that cancers emerged after ~1.5 years supports the hypothesis that **insulin therapy does not CAUSE cancer, it may just promote its development (and the insulin analogues MAY do it more than human insulins)**

**So what do we do next AND what do we tell patients?**

- This issue requires more research and Health Canada is warranted in studying it further.
- We should tell pts that this info is VERY preliminary & they should NOT stop taking their insulin glargine or detemir (uncontrolled sugars also have severe consequences).
- It is in nobody's best interest to start a witch-hunt against insulin glargine (and switching to detemir would make no sense as it would be expected to act similarly to glargine).
- **Keep in mind that: (1) human insulins** (e.g., Humulin N) **have been used for decades** and their safety profile is well-known; **(2) long acting insulin analogues** (e.g., glargine, detemir) are expensive and are NOT more effective than human insulins, they only have somewhat lower risk of nocturnal hypoglycemia.
- **Therefore, although this cancer data is preliminary, it is one more reason to use human insulins as the mainstay of therapy and to consider the analogues only in pts having trouble with hypoglycemia**

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<http://www.medicine.usask.ca/family/newsletters/rapid-rx>

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