

# Hedgehog Pathway Inhibitors Knocking Out BCC

BY SHERRY BOSCHERT

FROM THE ANNUAL MEETING OF THE  
PACIFIC DERMATOLOGIC ASSOCIATION

PASADENA, CALIF. – Two drugs – one old, one new – are showing promise in early clinical trials for the treatment of basal cell carcinomas.

If they prove to be useful, clinicians can thank scientists who successfully identified abnormalities in the hedgehog

signaling pathway as the mechanism of disease for basal cell carcinoma (BCC), Dr. Jean Tang said at the meeting.

“Every major pharmaceutical company is now interested in the hedgehog pathway, so we may see a lot of treatments in the near future” for BCC and other cancers, said Dr. Tang of Stanford (Calif.) University.

She and her associates are conducting a phase II trial of the experimental

Genentech drug GDC-0449 in patients with many BCCs from basal cell nevus syndrome (Gorlin’s syndrome), and a separate proof-of-concept study of the antifungal drug itraconazole in patients with small numbers of BCCs who do not have basal cell nevus syndrome.

For GDC-0449, a previous phase I study in 33 patients with locally advanced or metastatic BCC who took the drug for a median of 10 months found that 50%-

60% had partial or complete responses and the drug was generally well tolerated (N. Engl. J. Med. 2009;361:1164-72).

Of the 41 patients with basal cell nevus syndrome recruited thus far for the phase II trial – and randomized to 18 months of treatment with GDC-0449 or placebo – 23 patients (with 953 BCC tumors) have more than 1 month of data.

Although the study is still blinded, 15 patients in group A have developed a me-

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### Warnings and Precautions (cont'd)

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Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus®, and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus® dose may be required in patients with renal or hepatic impairment.

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dian of one new BCC during that month, compared with a median of 10 new BCCs in each of the 8 patients in group B, a significant difference that suggests group A may have received the drug and it may be working, Dr. Tang suggested.

In group A, patients started with a median of 252 BCCs and had 127 at the most recent follow-up, a 50% decline. In group B, patients started with 217 BCCs and had 267 at follow-up, a 23% increase in BCCs.

The difference between groups is significant, she said. Existing BCCs in group A also seem to have decreased in size.

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it has changed their lives," Dr. Tang said. "We are really excited about it."



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DR. TANG

Patients in group A, however, were significantly more likely to develop dys-

geusia (decreased taste sensation). The condition was seen in 14 of 15 patients, compared with none in group B. Seven patients in group A and none in group B reported some hair loss, though this difference was not statistically significant. Two patients in group A stopped treatment because of dysgeusia and hair loss, compared with none in group B.

These side effects may be acceptable to patients with basal cell nevus syndrome but probably not to patients with only one or two BCCs, Dr. Tang noted.

For the latter group, a proof-of-concept trial has randomized eight patients

thus far to 1 month of treatment with 400 mg/day of oral itraconazole, a drug that has been on the market for approximately 2 decades and is considered relatively safe, she said. Patients are followed clinically for changes in their BCCs, and they undergo tumor biopsies before and after the 1-month therapy to measure the treatment's effects on the hedgehog signaling pathway.

Preliminary data are "somewhat promising" in reducing BCC size, Dr. Tang said. The effect has not been as dramatic as with the GDC-0449 study, but neither have the side effects. ■

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**Important Safety Information for Lantus<sup>®</sup>** (insulin glargine [rDNA origin] injection) (cont'd)

### Drug Interactions

Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

### Adverse Reactions

Other adverse reactions commonly associated with Lantus<sup>®</sup> are injection site reaction, lipodystrophy, pruritus, and rash.

**Please see brief summary of full prescribing information for Lantus<sup>®</sup> on the following pages.**

<sup>a</sup>Glucose control defined as A1C <7%.

<sup>b</sup>Including diet, exercise, and other diabetes medications.

**References:** 1. Holman RR. *Diabetes Res Clin Pract.* 1998;40(suppl):S21-S25. 2. Polonsky WH, Jackson RA. *Clin Diabetes.* 2004;22(3):147-150. 3. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB. *Diabetes Care.* 2008;31(1):81-86. 4. Brown JB, Nichols GA, Perry A. *Diabetes Care.* 2004;27(7):1535-1540. 5. Data on file, sanofi-aventis U.S. LLC.

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