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# Industry Relationships

## Meenal Kheterpal, M.D.

### DISCLOSURES

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# Libtayo in Gorlin syndrome

## LIBTAYO/ Cemiplimab

A Phase 2 study was done on patients with either:

1. Advanced BCCs and locally advanced BCCs: single large tumors causing pain, bleeding and other problems

**OR**

2. Metastatic BCCs (spread to other organs in the body like lymph nodes and lungs) that had
- Progressed or did not respond to hedgehog pathway inhibitors (Odomzo or Erivedge)
  - In patients that did not tolerate these drugs

- **9 out of 132 patients in this trial had a diagnosis of Gorlin Syndrome**
- Of these 9 patients with Gorlin syndrome
  - **1** was noted to have **partial reduction of tumor**
  - **6** patients had **stable disease = no significant improvement / change in tumor size**
  - **2** patients had growth in **tumor size [3]**

**• Overall, patients with Gorlin syndrome did not respond as well to Libtayo compared to those without Gorlin syndrome, but the number of patients was low.**

### REFERENCE LIST

1. LIBTAYO® (cemiplimab-rwlc) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc./sanofi-aventis U.S. LLC.
2. PD-1 in Patients With Advanced Basal Cell Carcinoma Who Experienced Progression of Disease on Hedgehog Pathway Inhibitor Therapy, or Were Intolerant of Prior Hedgehog Pathway Inhibitor Therapy. ClinicalTrials.Gov website. <https://clinicaltrials.gov/ct2/show/NCT03132636> Accessed on January 7, 2021.
3. Data on File. Regeneron Pharmaceuticals, Inc.

# Libtayo in Gorlin syndrome

## Libtayo/Cemiplimab

**DOSING:** 350mg every 3 weeks by IV infusion over 30 minutes ( $\pm 10$  minutes) for up to 93 weeks (nearly 2 years)

During this trial, BCCs were evaluated with measurements and photographs at the end of each 9-week cycle for the first 5 cycles, then every 12 weeks for cycles 6-9

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1. LIBTAYO® (cemiplimab-rwlc) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc./sanofi-aventis U.S. LLC.
2. PD-1 in Patients With Advanced Basal Cell Carcinoma Who Experienced Progression of Disease on Hedgehog Pathway Inhibitor Therapy, or Were Intolerant of Prior Hedgehog Pathway Inhibitor Therapy. ClinicalTrials.Gov website. <https://clinicaltrials.gov/ct2/show/NCT03132636> Accessed on January 7, 2021.
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# Trial Characteristics

- Median age: 68.0, youngest person was 38 years old
- 89% were men
- Mostly caucasians, healthy
- 100% had previously taken Hedgehog Inhibitor
- 75% had growth in tumors while on Hedgehog Inhibitor
- Most (72%) had BCCs on their head and neck, 23% had them on their trunk (back and stomach areas)
- There were two groups of patients:
  1. Patients with locally advanced BCCs (laBCC) that have not spread to other organs.
  2. Patients with metastatic BCCs (mBCC). These have spread to other organs in the body like lymph nodes and lungs.

# Reasons for Discontinuation of Libtayo

The MOST common reason for premature treatment discontinuation in the trial was  
**PROGRESSION OF DISEASE**

- **Progression of disease occurred in half of the patients in metastatic BCC trial group**
- **Progression of disease occurred in on-third (34%) of the patients locally advanced (large but not metastatic) BCCs**

- In the group with metastatic BCCs, 2/3 (66.7%) stopped the treatment for several reasons.
  - Half of this group stopped due to progression of disease.
- In the group with locally advanced BCC, 61.9% discontinued the treatment for several reasons.
  - One-third (34%) of these patients stopped due to progression of disease.

# Side Effects of Treatment

Unleashing the immune system may lead it to attack normal tissues.

- The most common adverse reactions (reported in at least 15% of patients)
  - **Fatigue**
  - **Joint aches**
  - **Diarrhea**
  - **Rash**
  - **Itching**
  - **Common cold**
- Nearly **1 in 3** patients receiving Libtayo in the trial (**32%**) developed serious adverse reactions to the medication.
- The most common serious adverse events were as follows:
  - Colitis (bloody diarrhea)
  - Impaired kidney function shown in blood work
  - Adrenal gland issues (Addison's Disease = inadequate amount of hormones are released from these glands.)
  - Anemia - low blood count
  - Infections
  - Fatigue / sleepiness

# Side Effects of Treatment, continued

Unleashing the immune system may lead it to attack normal tissues.

- **Fatal adverse reactions occurred in 1.5% of patients** who received LIBTAYO (acute kidney failure and failure to thrive).
- Some side effects may be permanent (lifelong), others may disappear over time after Libtayo is stopped.
- Permanent discontinuation of Libtayo due to an adverse reaction occurred in **13% of patients**.  
**Bloody diarrhea and general physical health deterioration** is what led to this stoppage in most participants.



# Results : Duration of Response

- In patients with metastatic BCC (mBCC), **no one had their disease cured.**
    - 21% (1 in 5 patients) had some shrinkage in their tumors or no further growth
  - In locally advanced BCCs (laBCC), **5 (3.8 %) patients had cures**
    - 31% (1 in 3) had some shrinkage in their tumors or no further growth
- 
- Median duration of follow-up was:
    - **15.6 months** (range: 0.5–25.1) among patients with laBCC
    - **9.5 months** (range: 1.5–27.2) among patients with mBCC

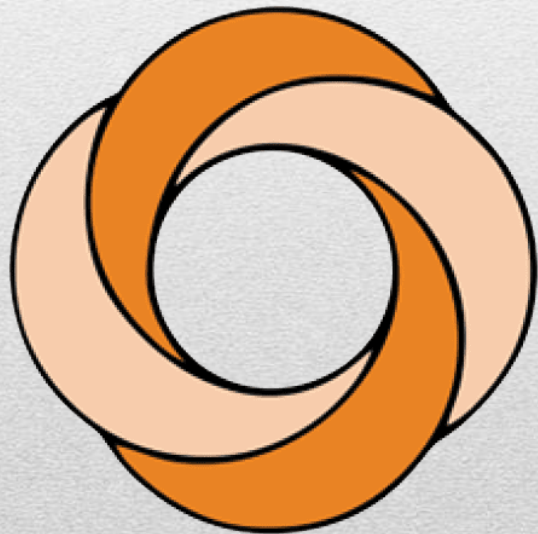
## In Conclusion: What if You Respond to Libtayo?

When asked, the patients (up to 31%) in the study who responded to Libtayo and had advanced BCCs felt that they had "maintained or improved their symptoms, functioning, and quality of life".

# Treatment: Pros and Cons

Treatment	Pros	Cons
<b><u>Odomzo</u></b> <b>(Sonidegib)</b>	<ul style="list-style-type: none"><li>• Shrinks BCCs</li><li>• Shown to be effective in GS</li><li>• Effective in treating locally aBCCs</li></ul>	<ul style="list-style-type: none"><li>• Side effects</li><li>• BCCs may come back</li></ul>
<b><u>Erivedge</u></b> <b>(Vismodegib)</b>	<ul style="list-style-type: none"><li>• Shrinks BCCs</li><li>• Shown to be effective in GS</li><li>• Effective in treating metastatic BCCs</li></ul>	<ul style="list-style-type: none"><li>• Side effects</li><li>• BCCs may come back</li></ul>
<b><u>Libtayo</u></b> <b>(Cemiplimab)</b>	<ul style="list-style-type: none"><li>• Shrinks BCCs</li><li>• Effective in treating metastatic BCCs</li></ul>	<ul style="list-style-type: none"><li>• Lower response rate in BCC size reduction</li><li>• Side effects may be severe, permanent, life altering</li><li>• Uncertain effectiveness in GS</li><li>• Unknown recurrence rate of BCCs in GS</li></ul>

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