Rationale

Opioid medications are the mainstay of treatment for severe, chronic cancer pain. The analgesic activity of opioids is mediated via central mu opioid receptors (MORs) in the central nervous system. However, MORs are also present on endothelial cells and in human tumors (peripheral MORs), including lung cancer. Expression and activation of peripheral MORs are associated with tumor progression in animal models. Recent clinical studies raise the possibility that opioid exposure is also associated with tumor progression in patients with various malignancies including lung cancer. Symptoms related to progression of cancer and its treatments, as well as the adverse effects of opioids, all contribute to impair the health-related quality of life (HRQoL). One recent trial studied people with very advanced cancers who were constipated from opioids. Those who got a medication that blocks unwanted peripheral opioid effects lived significantly longer than patients who did not get the medication. However, it is NOT known if opioids stimulate cancer growth in people.

Our long-term goal is to develop a novel, non-chemotherapeutic intervention blocking the activation of peripheral opioid receptors that contributes to tumor progression and adverse effects of opioids. This may improve the HRQoL of patients with advanced malignancies, and may also improve disease outcomes. Towards this eventual goal, we will perform this pilot study to first determine the feasibility and safety of long-term administration of an orally available, FDA-approved, peripherally acting mu opioid receptor antagonist (PAMORA) in a patient population receiving standard chemotherapy for advanced, incurable lung cancer.
Alliance A221504: A Randomized, Double-Blind, Placebo-Controlled Pilot Study of an Oral, Selective Peripheral Opioid Receptor Antagonist in Advanced Non-Small Cell Lung Cancer

Pankaj Gupta, MD
VA Long Beach Health Care System, Long Beach, CA

Primary
- To determine feasibility and safety of long-term administration of naloxegol in patients with advanced NSCLC receiving first-line systemic therapy

Secondary
- HRQoL
- Pain levels and analgesic requirements
- Opioid adverse effects
- Progression free survival (PFS) and overall survival (OS)
- Chemotherapy discontinuation rate due to AEs
- Deaths attributable to chemotherapy
Data collection every 3 weeks for 1 year (at clinic visit or by mail).
Blood samples: once at 3 and 6 weeks from initiation of study treatment
N = 204. Study duration 2 years
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Rationale
Objective
Study Schema
Eligibility Criteria
Follow Up

Please use the headings above to navigate through the different sections of the poster

Treatment Plan

<table>
<thead>
<tr>
<th>Bottle 1</th>
<th>Bottle 2</th>
<th>Naloxegol Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>“12.5 mg”</td>
<td>“25 mg”</td>
<td>12.5 mg</td>
</tr>
<tr>
<td>12.5 mg Naloxegol</td>
<td>25 mg Placebo</td>
<td>12.5 mg</td>
</tr>
<tr>
<td>12.5 mg Placebo</td>
<td>25 mg Naloxegol</td>
<td>25 mg</td>
</tr>
<tr>
<td>12.5 mg Placebo</td>
<td>25 mg Placebo</td>
<td>0 mg</td>
</tr>
</tbody>
</table>

Take one pill from each of the two bottles, once every day

Naloxegol is FDA approved for opioid-induced constipation. Does not interfere with pain relief from opioids. Generally well tolerated. Stored at room temperature. It is not a controlled substance.
Naloxegol and placebo are provided by AstraZeneca. Standard evaluation, cancer treatment, and monitoring of advanced lung cancer should be billable to Medicare/insurers, per CTSU.
Eligibility Criteria

- Patients with stage IIIB or IV (AJCC 7th ed) non-small cell lung cancer (NSCLC: any subtype) starting any first-line systemic therapy of the investigator’s choice
- No known EGFR or EML4-ALK driver mutations (no need to test just for this study)
- Maintenance treatment OK. Prior adjuvant chemo/radiation, palliative radiation OK
- Performance status ECOG 0-2
- Some opioid use (no minimum amount) at some time during 4 weeks prior to registration: see list of allowed and prohibited opioids
- Patients with treated brain metastases eligible
- A221504 does not prohibit patients from participating concurrently in another study/trial, as long as the other trial allows participation in A221504
Alliance A221504: 
A Randomized, Double-Blind, Placebo-Controlled Pilot Study of an Oral, Selective Peripheral Opioid Receptor Antagonist in Advanced Non-Small Cell Lung Cancer

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Eligibility Criteria

Patients can be registered for up to 4 weeks PRIOR to starting the first cycle of systemic therapy or any time within 12 weeks AFTER starting systemic therapy.

Start date of first cycle of first line systemic therapy

| 4 weeks | 12 weeks |

Subjects who have already started first line systemic therapy can register on study any time within 12 weeks after starting systemic therapy. Subjects who first register on study can start first line systemic therapy any time within 4 weeks after registering.
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