Patidegib Gel Clinical Trial for BCC Prevention

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Disclosures

• Founder, Board of Directors, Stockholder and Consultant: PellePharm

• Consultant: Genentech, Menlo Therapeutics, Phoenix Tissue Repair

• I will discuss the off-label use of vismodegib
30 years to make the first Hedgehog Pathway inhibitor

1970s • Isolation of genes that control development of anterior-posterior body axis of *Drosophila*
  • *Drosophila* and vertebrate HH: gene isolation, HH protein biogenesis, cyclopia in *Shh* mutants

1990s • Identification of PTCH and SMO mutations in heritable and sporadic forms of BCC

2005 • Identification of cyclopaamine as 1st small molecule HH inhibitor

2007 • First mouse model of BCC
  • Randomized trials of vismodegib (oral)

2012 • Vismodegib approval for advanced/metastatic BCC

2015 Patidegib topical gel for BCCs in Gorlin Syndrome
## Overview of Prior Patidegib Topical Gel Clinical Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Outcome</th>
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| Ph 2a: 2% and 4% BID to face  
*UK study in Gorlin Syndrome (201)* | Double-blind, randomized, placebo-controlled trial (n=17) for 6 months | CR and **fewer tumors** seen in treatment groups; reduction in tumor size seen in 2% BID group; little evidence of systemic AEs commonly experienced with oral HH inhibitors. More skin AEs in 4% |
| Ph 2 : 2% and 4% QD and BID to nodular BCC  
*US study in sporadic BCCs (202)* | Double-blind, dose-escalating, randomized, placebo-controlled trial (n=36) for 3 months | Reduction in Gli biomarker for 2% and 4% QD cohorts and significant **tumor reduction in 2% QD cohort**; clinical and histological CR seen in 2% QD and 2% BID cohorts. More skin AEs in 4% |
| MUSE study: 4% gel to 25% BSA (101) | Open label healthy volunteer study (n=22) for 2 weeks | Mild irritation and erythema. No systemic AEs commonly experienced with oral HH inhibitors |
Phase 2a Trial: Study design and endpoints

• Proof of concept, small trial with 17 trial participants for 26 weeks applied to 5 target lesions and to entire face for field treatment:
  • 2% patidegib topical gel BID, 6 trial participants with 24 evaluable tumors
  • 4% patidegib topical gel BID, 6 trial participants with 24 evaluable tumors
  • Vehicle gel BID, 5 trial participants with 20 evaluable tumors
• Primary endpoints: % decrease in diameter of 5 target tumors at end of 26 weeks, GLI1 reduction (measure of potential anti-tumor activity), safety
• Secondary endpoints:
  • Number of new SEBs (surgically-eligible BCCs) on face, proportion of BCCs that grew to SEB size
  • Change in tumor size of target SEBs and BCCs
Gorlin Phase 2: Target SEBs with Clinical clearance observed in treatment groups only (none in vehicle)

- Complete clinical response
- No irritation or itch

2% treatment group, subject 01-012

- Complete clinical response
- No irritation or itch

4% treatment group, subject 01-013

- Complete and partial clinical responses

4% treatment group, subject 01-007
Phase 2 Gorlin UK: Number of nSEBs per trial participant in ITT and Per Protocol analysis (secondary endpoint)

- 1.4 new tumors in vehicle patients vs. 0.4 new tumors in drug treated (ITT)
- 1.4 new tumors in vehicle patients vs. 0.3 new tumors in drug treated (PP)
Summary of 3 clinical trials

• Patidegib topical 2% BID dose may have the potential to reduce number of new SEBs
• 2% with no significant skin irritation
• Topical 2 and 4% lead to <500-fold systemic exposure compared with oral and have little evidence of oral Hedgehog pathway inhibitor side effects
• Phase 3 trial clinical trial in Gorlin Syndrome initiated to reduce disease burden of SEBs
  • Comparison: 2% BID vs. Vehicle gel BID on the face for 12 months
# Phase 3 Trial in BCNS (Gorlin Syndrome)

<table>
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<tr>
<th>Title</th>
<th>A Multicenter, Randomized, Double-blind, Vehicle-controlled, Phase 3 Efficacy and Safety Study of Patidegib Topical Gel, 2%, for the Reduction of Disease Burden of Persistently Developing Basal Cell Carcinomas (BCCs) in Subjects with BCNS</th>
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<tbody>
<tr>
<td>Investigational Product</td>
<td>Patidegib Topical Gel, 2% (w/w), or Topical Gel, Vehicle</td>
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<tr>
<td>Study Population</td>
<td>Participants with moderate to severe BCNS, defined as history of ( &gt;10 ) BCCs over last 2 years (including ( &gt;3 ) small BCCs on the face) plus 2 BCCs less than 5mm currently on the face</td>
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<tr>
<td>Number of Subjects</td>
<td>N=126 evaluable subjects (150 target enrollment) in 2 arms: Patidegib Topical Gel, 2%, and Vehicle with a 1:1 randomization</td>
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<td>Primary Endpoint</td>
<td>The number of new surgically eligible BCCs (nSEBs) per subject by month 12</td>
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<td>Study Design</td>
<td>• Approximately 50 sites in US, Canada and EU</td>
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www.gorlinstudy.com