Study protocol

Title: Efficacy and safety of Sonic Hedgehog Inhibitors in Basal Cell Carcinomas: A Systematic Review and Meta-Analysis

Authors: Pingxing Xie and Philippe Lefrançois

Review questions: How effective are Sonic Hedgehog Inhibitiors (SHHi) for basal cell carcinomas (BCC) as a class? How common are side effects with Sonic Hedgehog Inhibitiors (SHHi) for basal cell carcinomas (BCC) as a class?

Databases: Our search is to find all trials and studies using SHHi in BCC. We will use ClinicalTrials.gov to determine which SHHi had been used for BCC. We will perform a broad search in PubMed, ClinicalTrials.gov, Embase and Cochrane Central Register of Clinical Trials in September 2016. The search will be repeated monthly until the end of year 2016 to check for newer publications. References in the selected articles will be scanned for missing articles.

Types of studies and Study selection: We will include clinical trials, prospective case series, and retrospective medical record reviews using SHHi in BCC on human subjects, published in English. Case reports will be excluded. Studies providing only outcomes post-surgery or post-radiation therapy will be removed. Studies of SHHi concurrently with an additional treatment will also be removed. Studies without quantitative measurements will not yield any data, thus they will be excluded. For efficacy, numbers to calculate Overall Response Rates and Compete Response Rates are required for inclusion. For safety, side effects will need to be directly related to SHHi.

Condition: Cutaneous Basal Cell Carcinoma (BCC) treated with Sonic Hedgehog Inhibitors (SHHi).

Participants: Patients with Cutaneous Basal Cell Carcinoma (BCC) treated with Sonic Hedgehog Inhibitors (SHHi). Patients receiving concurrent treatment with another modality will be excluded. Patients with outcomes measured post-surgery or post-radiation therapy will not be included either, they will only be part of the meta-analysis if outcomes post-SHHi and prior to surgery/radiation therapy are measured.

Interventions: Treatment with SHHi.

Comparator: No placebo group.

Context: Any studies fitting the aforementioned criteria will be considered for inclusion.

Outcomes:

Primary: Observed Response Rates (ORR), Complete Response Rates (CRR), Prevalence of major side effects

Secondary: Clinical Benefit Rates (CBR)

Data extraction: Two investigators will extract efficacy and safety data independently using a standardized Excel form. Variables to be extracted include study reference, study name, type of trial, molecule, posology, response criteria, number of patients, number of patients experiencing major side effects, number of patients with complete response, number of patients with partial response, number of patients with stable disease, number of patients with disease progression, median follow-up in study, median drug exposure in study, presence of industry sponsorship, presence of placebo group, presence of blinding, and a free text section for biases.

Bias assessment: Two investigators will independently assess the quality of evidence, publication bias, industry involvement, study heterogeneity, and quality of response criteria.

Data analysis: We will perform a meta-analysis for SHHi as a class, combining results from SHHi studied in BCC. We will use fixed-effects linear models. We will model variance as needed. We will use Bayesian models with random-effects for sensitivity. Funnel plots and trim-and-fill method will be used for publication bias. I2, Forest plots and sensitivity analyses will be used for assessing heterogeneity. All analyses will be performed in R.

Subgroup analyses: None planned.

Publication: Top dermatology, oncology or internal medicine journals.

Contact person: Philippe Lefrançois [philippe.lefrancois2@mail.mcgill.ca](mailto:philippe.lefrancois2@mail.mcgill.ca)

Dermatology Resident – McGill University

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