

## **SUPPLEMENTARY MATERIAL**

### **Canadian Expert Consensus Recommendations on the Use of Photodynamic Therapy in Actinic Keratosis**

Vimal H. Prajapati<sup>1-6</sup>; Vincent Richer<sup>7,8</sup>; Megan Sander<sup>4</sup>; Alim R. Devani<sup>4,5</sup>; Sonya Abdulla<sup>9,10</sup>; Maxwell Sauder<sup>11</sup>; Simon Nigen<sup>12,13</sup>; Ivan V. Litvinov<sup>14,15</sup>; Charles W. Lynde<sup>16-18</sup>; Jaggi Rao<sup>19</sup>

<sup>1</sup> Division of Dermatology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada

<sup>2</sup> Section of Community Pediatrics, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada

<sup>3</sup> Section of Pediatric Rheumatology, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada

<sup>4</sup> Skin Health & Wellness Centre, Calgary, Alberta, Canada

<sup>5</sup> Dermatology Research Institute, Calgary, Alberta, Canada

<sup>6</sup> Probit Medical Research, Calgary, Alberta, Canada

<sup>7</sup> Pacific Derm, Vancouver, British Columbia, Canada

<sup>8</sup> Department of Dermatology and Skin Science, University of British Columbia, Vancouver, British Columbia, Canada

<sup>9</sup> Dermatology on Bloor, Toronto, Ontario, Canada

<sup>10</sup> FACE Toronto and Women's College Hospital, Toronto, Ontario, Canada

<sup>11</sup> University of Toronto, Toronto, Ontario, Canada

<sup>12</sup> Division of Dermatologie, McGill University Health Centre, Montréal, Québec, Canada

<sup>13</sup> Sima Recherche, Verdun, Québec, Canada

<sup>14</sup> Department of Specialized Medicine (Dermatology), St. Mary's Hospital Centre, McGill University, Montréal, Québec, Canada

<sup>15</sup> St. Mary's Research Centre, Montréal, Québec, Canada

<sup>16</sup> Division of Dermatology, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

<sup>17</sup> The Lynde Institute for Dermatology & Lynderm Research Inc., Markham, Ontario, Canada

<sup>18</sup> Probit Medical Research Inc., Markham, Ontario, Canada

<sup>19</sup> Division of Dermatology, University of Alberta, Edmonton, Alberta, Canada

#### **Corresponding Author**

Vimal H. Prajapati, MD, FRCPC, DABD  
Dermatology Research Institute  
Suite 310, 8500 Blackfoot Trail S.E.  
Meadows Mile Professional Building  
Calgary, Alberta, Canada T2J 7E1  
Email: vimal@dermatologyresearch.ca

## **Supplementary Appendix 1. Literature search strategy used to inform statement development**

A targeted literature review was conducted to inform development of the draft consensus statements for this modified Delphi process. The review was intended to identify key guidelines, randomized and nonrandomized clinical studies, systematic reviews, and meta-analyses relevant to the use of photodynamic therapy (PDT) in actinic keratosis (AK), including disease framing, lesion- versus field-directed treatment strategies, PDT modalities and protocols, special populations, and combination approaches.

The literature search was performed in PubMed/MEDLINE and was limited to English-language publications. The search covered publications from 2005 onward, with emphasis on evidence published between 2010 and 2025 to reflect contemporary clinical practice. The final literature search was run on October 10, 2025. Applied filters included Humans, Adult, and the following article types where applicable: guidelines, clinical trials (phase II to III), randomized controlled trials, systematic reviews, meta-analyses, and observational studies.

The following core searches were used:

### **Search 1. AK guidelines and treatment landscape**

("actinic keratosis"[MeSH Terms] OR "actinic keratosis"[Title/Abstract] OR "solar keratosis"[Title/Abstract])  
AND  
(guideline[Publication Type] OR "practice guideline"[Title/Abstract] OR "consensus"[Title/Abstract] OR "systematic review"[Title/Abstract])

### **Search 2. PDT for AK, general**

("actinic keratosis"[MeSH Terms] OR "actinic keratosis"[Title/Abstract])  
AND  
("photodynamic therapy"[MeSH Terms] OR "photodynamic therapy"[Title/Abstract] OR PDT[Title/Abstract])  
AND  
(topical[Title/Abstract] OR aminolevulinic[Title/Abstract] OR methyl aminolevulinate[Title/Abstract])

### **Search 3. Daylight versus conventional PDT**

("actinic keratosis"[Title/Abstract])  
AND  
("photodynamic therapy"[Title/Abstract] OR PDT[Title/Abstract])  
AND  
(daylight[Title/Abstract] OR "daylight PDT"[Title/Abstract] OR "conventional"[Title/Abstract] OR "red light"[Title/Abstract])

### **Search 4. Special populations and combination regimens**

("actinic keratosis"[Title/Abstract])  
AND  
("photodynamic therapy"[Title/Abstract] OR PDT[Title/Abstract])

AND

(transplant[Title/Abstract] OR "solid organ transplant"[Title/Abstract] OR immunosuppressed[Title/Abstract] OR "5-fluorouracil"[Title/Abstract] OR "combination"[Title/Abstract])

Retrieved publications were reviewed by the steering committee and selected for relevance to the predefined domains and draft statement topics. Included publications were used to support development, refinement, and rationale writing for the draft consensus statements. Reference lists of key guidelines, reviews, and pivotal trials were also examined to identify additional relevant publications. The search was designed as a targeted literature review to support consensus development, rather than as a formal systematic review. This approach was intended to ensure that the evidence base was transparent and reproducible, such that a dermatologist using PubMed could broadly replicate the search strategy.

**Supplementary Table 1.** Selected randomized controlled trials of conventional ALA- and MAL-based photodynamic therapy for actinic keratosis

| Study                                 | Study design and population                                                                                                                                                                            | Treatment regimen                                                                                                                                                                                            | Key efficacy results                                                                                                                                                                                                                                         |
|---------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Piacquadio et al., 2004 <sup>24</sup> | Two identical, investigator-blinded, randomized, vehicle-controlled, phase III multicentre trials; 243 patients with 4–15 AKs on the face or scalp. Very hyperkeratotic grade 3 lesions were excluded. | ALA 20% topical solution or vehicle applied to individual lesions, followed 14–18 hours later by blue-light illumination at 10 J/cm <sup>2</sup> . Residual lesions were eligible for retreatment at week 8. | At week 12, patient complete clearance was 73% with ALA-PDT versus 8% with vehicle. Lesion complete clearance was 91% versus 25%. Week 12 results included 30% of patients treated with ALA who received a second treatment.                                 |
| Szeimies et al., 2010 <sup>26</sup>   | Randomized, double-blind, placebo-controlled, phase III multicentre trial; 122 patients with 4–8 mild-to-moderate AKs on the face and/or bald scalp.                                                   | BF-200 ALA gel or placebo with 3-hour incubation, followed by red-light illumination using the Aktilite CL128 or PhotoDyn 750. Residual lesions were retreated after 12 weeks.                               | After up to two treatments, patient complete clearance was 64% with BF-200 ALA versus 11% with placebo, and lesion complete clearance was 81% versus 22%. Outcomes varied by light source.                                                                   |
| Reinhold et al., 2016 <sup>25</sup>   | Randomized, double-blind, placebo-controlled, parallel-group, phase III multicentre trial; 87 randomized patients with 4–8 mild-to-moderate AKs within defined fields on the face and/or scalp.        | Field-directed BF-200 ALA gel or placebo with 3-hour incubation, followed by BF-RhodoLED red-light illumination at 37 J/cm <sup>2</sup> . Residual lesions were retreated after 12 weeks.                    | After a maximum of two treatments, patient complete clearance was 91% with BF-200 ALA versus 22% with placebo, and lesion complete clearance was 94.3% versus 32.9%. After one treatment, the corresponding rates were 62% versus 9% and 84.2% versus 22.0%. |
| Pariser et al., 2003 <sup>23</sup>    | Prospective, randomized, double-blind, placebo-controlled multicentre trial; 80 patients with 4–10 mild-to-moderate, nonpigmented AKs on the face or scalp.                                            | MAL 160 mg/g cream or placebo applied under occlusion for 3 hours, followed by noncoherent red-light illumination at 75 J/cm <sup>2</sup> . Treatment was repeated after 1 week.                             | Complete lesion response at 3 months was 89% with MAL-PDT versus 38% with placebo. Good or excellent cosmetic outcomes were reported in more than 90% of patients treated with MAL-PDT.                                                                      |