The first patient was a 40-year-old man with a 4-year history of transformed MF with lymph node involvement (International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer stage N3). There was 15% CD30 expression on the lymph node core needle biopsy sample. He had received several treatment lines: chemotherapy (CHOP), bexarotene, interferon alpha, methotrexate. A year and a half after disease onset, it was finally decided to initiate brentuximab (six infusions at a dose of 1·8 mg kg^{-1}), which induced a complete clinical response allowing ASCT with a sibling donor. One week after the transplant, a recurrence of the transformed MF lesions was observed. The patient also developed severe chronic cutaneous, pulmonary and hepatic graft-versus-host disease, which was treated with oral corticosteroids. The resumption of BV for six infusions (dose decreased to 1·2 mg kg^{-1} due to peripheral neuropathy) then allowed complete remission. A relay by liposomal doxorubicin (four infusions) was finally performed due to the worsening of neuropathy, followed by a maintenance treatment with bexarotene at a dose of 260 mg m^{-2} day^{-1} (525 mg). Two years after resumption of treatment the patient was still in complete remission and there was no recurrence.

The second patient was a 62-year-old male treated for stage IIB, transformed MF over the past 9 years with initial CD30 expression at 5%. He had received several treatment lines: interferon alpha, phototherapy, bexarotene, methotrexate, liposomal doxorubicin, romidepsin, gemcitabine, ifosfamide/etoposide, vinblastine. Due to progressive disease 8 years after the initial diagnosis with an increase in CD30 expression on the last skin biopsy sample (25% of lymphoid cells), BV was introduced with a very good partial response allowing haploidentical ASCT after six infusions at a dose of 1·8 mg kg^{-1}. One and a half months after the transplant, a recurrence of the transformed MF lesions was observed. Peripheral blood chimerism showed 100% recipient-derived cells. A resumption of BV then allowed a complete remission after four infusions (dose decreased to 1·2 mg kg^{-1} due to peripheral neuropathy) and a maintenance treatment with bexarotene at a dose of 225 mg m^{-2} day^{-1} (450 mg). Five months after resumption of BV, the patient was still in complete remission and there was no recurrence.

BV was effective rapidly in our two patients suffering from transformed MF for several years, before and after ASCT. By its dramatic efficacy on transformed disease, BV confirms its usefulness as a bridge to ASCT. Moreover, BV is also effective and seems well tolerated after transplant, either in the treatment of an early recurrence or perhaps as a consolidation treatment as recently reported in the context of Hodgkin lymphoma.[7,9] The main limitation of treatment remains the development of neuropathy.

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Rosacea treatment guideline for the Netherlands*

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Linked Editorial: van Zuuren *et al.* Br J Dermatol 2020; **182**:1319–1320.

Dear Editor, The classification of rosacea has evolved from a subtyping into a phenotype approach,[1–3] and an updated

systematic review on interventions in rosacea using this approach was recently published.[4] Therefore, we developed a new evidence-based guideline for all physicians and skin therapists involved in the management of patients with rosacea. A patient information leaflet based on this guideline was produced. The working group (WG) consisted of four dermatologists, two general practitioners, one ophthalmologist, one plastic surgeon, two skin therapists, one patient and two staff members of the Dutch Society of Dermatology and Venereology. All affiliated organizations participated in external review. The Dutch Association for Hospital Pharmacists was invited to participate in the WG, but chose to participate only in the external review. The Association of Innovative Medicines, Dutch Health Insurers, the Dutch Association of Hospitals and the Dutch Federation of University Medical Centres were invited to participate in devising health questions and external review. Development of the guideline was independently funded by the Dutch Medical Specialists' Quality Fund. Two WG members had received one-off nonfinancial support from Galderma in 2016; the other members declared no conflicts of interest.

The updated systematic review 'Interventions for rosacea based on the phenotype approach' served as the basis for guideline development.[4] This review conformed to the PRISMA statement and included GRADE certainty-of-evidence assessments for all prespecified outcomes (quality of life, participant-assessed rosacea severity, adverse events, physician-assessed rosacea severity, erythema and telangiectasia, lesion counts, time to improvement, and duration of remission).[4,5] The search up to March 2018 provided 152 randomized controlled trials.[4] Study selection, data extraction, risk-of-bias assessment (Cochrane risk-of-bias tool) and analyses were carried out independently by two authors. The complete content of the review, encompassing 93 comparisons and including 25 summary-of-findings tables, is available in the appendix of that paper.[4] Three of the authors of this systematic review were involved in the development of the guideline (E.J.v.Z., M.M.D.v.d.L. and B.W.M.A.).

The health questions covered in the guideline, as formulated by the WG and external stakeholders, were (i) which self-care measures can be advised; (ii) what are the effectiveness and safety of the topical treatments brimonidine, oxymetazoline, ivermectin, metronidazole and azelaic acid, and how suitable are other topical treatments; (iii) what are the effectiveness and safety of tetracyclines and isotretinoin, and how suitable are other systemic treatments; (iv) what are the effectiveness and safety of intense pulsed light and laser-based therapies; (v) what are the effectiveness and safety of combination treatments; (vi) which therapeutic options exist for phymas; (vii) which self-care measures can be advised for ocular rosacea; (viii) what are the effectiveness and safety of treatment options for ocular rosacea; (ix) when do patients with ocular rosacea need to be referred to an ophthalmologist; (x) which therapeutic options are safe during pregnancy; (xi) which therapeutic options are safe for children; and (xii) what are the effectiveness and safety of maintenance treatments.

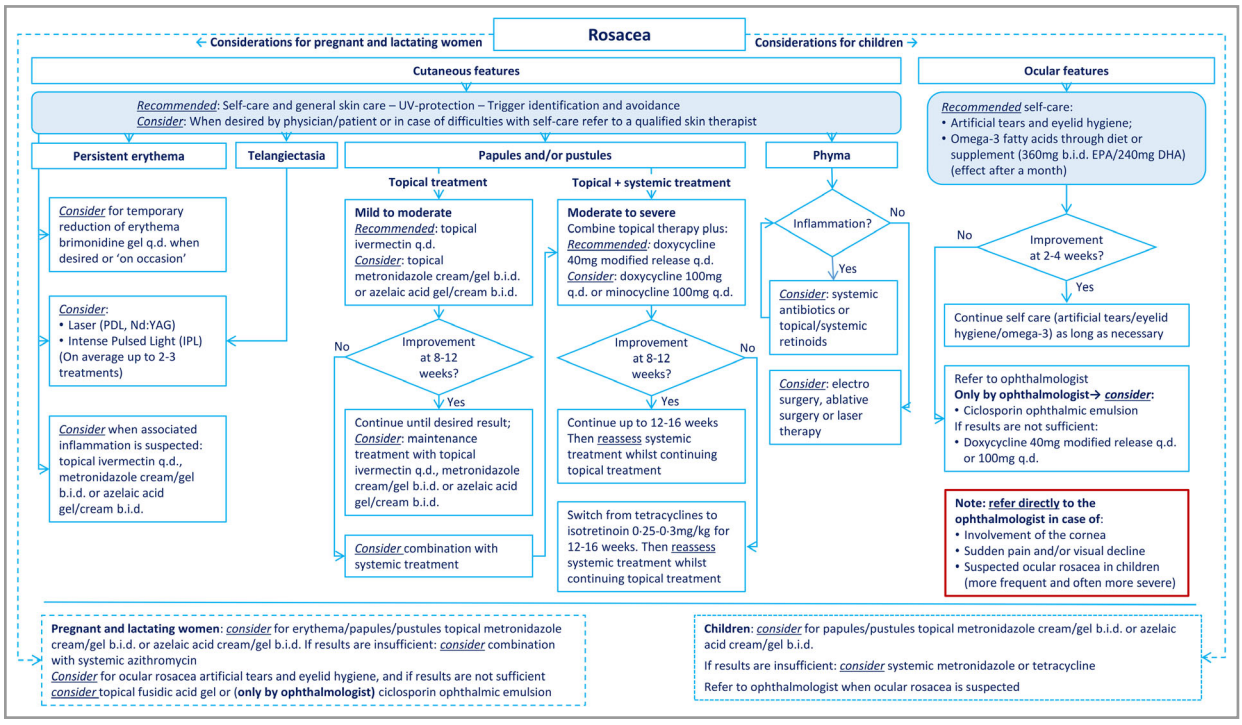

Fig 1. Rosacea treatment algorithm. Consider = weak recommendation. Recommended = strong recommendation. b.i.d., twice daily; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PDL, pulsed-dye laser; q.d., once daily; UV, ultraviolet; YAG, yttrium aluminium garnet.

The guideline followed the GRADE Evidence to Recommendation Frameworks. In making recommendations the WG integrated estimates of effect for desirable and undesirable outcomes of interest and confidence in the estimates of effect (certainty of evidence), items available from the systematic review, with estimates of values and preferences, and resource use.[6,7] Recommendations are either strong or weak, and for or against a treatment.[6] We used the wording 'recommend' for strong recommendations and 'consider' for weak recommendations. This guideline was developed for the Netherlands; however, its generalizability with respect to costs, availability and preferences may differ from country to country. To ensure completeness and transparency of reporting of the guideline the AGREE II checklist was used.[8]

Considering that rosacea has a negative impact on quality of life and that improvement of well-being is important, a full chapter was dedicated to this topic. The WG recommended addressing quality of life (aspects most bothersome to the patient), treatment satisfaction, social and professional functioning, and psychological well-being.

The most important recommendations have been reported in a treatment algorithm (Fig. 1). In addition to the recommendations provided in the treatment algorithm, the WG recommended against the use of topical clindamycin, solely or in combination with topical tretinoin. Due to inconsistent evidence regarding the effectiveness of benzoyl peroxide cream or gel and of permethrin cream, prescribing these warrants caution. The same holds true for oral azithromycin, although it could be a treatment option for those experiencing adverse events of doxycycline and minocycline, or in pregnant women. Topical oxymetazoline and minocycline foam are not yet available in the Netherlands, but were evaluated in the guideline (with the caveat of nonavailability). The full guideline is available at www.nvdv.nl.

The WG will consider an annual update or revision based on recent developments and new evidence. An updating process will be launched when required.

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**Plain language summary available online*