

Basal cell carcinoma and basal cell nevus syndrome

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Impact paragraph

The incidence of basal cell carcinoma (BCC) is high and expected to grow explosively in the next ten years. This may cause a major health issue in the near future, as a lot of surgical excisions will have to be performed to treat all the BCCs. Over the past decades, non-invasive treatments have been approved as therapy for BCC. The most effective, non-invasive, self-administered treatment for superficial BCC (sBCC) is imiquimod 5% cream, which is broadly accepted as standard treatment for sBCC. Imiquimod is an immunomodulator that binds to toll-like receptors 7 and 8.

We investigated the long-term effectiveness of imiquimod 5% cream in nodular BCC. Five years after treatment, the probability of remaining tumour-free in nodular BCC was 77.8% after treatment with curettage followed by imiquimod 5% cream and 98.2% after treatment with surgical excision. Although surgical excision is superior in efficacy, non-invasive therapy has several advantages, such as a better cosmetic outcome and the ability to treat multiple tumours at once in an at home setting. In nBCC patients who highly value cosmetic outcome, burden from surgery or have a preference for a treatment at home, imiquimod 5% cream is a good treatment option.

For a better understanding of the cause of treatment failure of imiquimod in approximately 20% of the patients, we analysed patient, tumour and treatment characteristics. Several predictors of treatment failure were found. Knowledge on predictors of treatment failure eventually leads to the possibility of determining which BCCs cannot be treated with imiquimod 5% cream before therapy is initiated. This knowledge may also be helpful in future studies aiming at improving treatment efficacy.

The high incidence of BCC will also lead to a rising incidence of patients with advanced BCC, which comprises both locally advanced and metastatic BCC. In part two of this thesis I describe a study on non-invasive treatment options in patients with advanced BCC. In this retrospective cohort study we investigated different aspects of treatment with the hedgehog pathway inhibitor vismodegib in all BCCs that received this treatment in the Netherlands. With this study, the real world use of this therapy was demonstrated, leading to a more strict protocol for treatment with hedgehog pathway inhibitors. This eventually resulted in a national prospective registry study in patients treated with hedgehog pathway inhibitors. Communication between different prescribing physicians and consequently more uniformity in prescription enables optimal treatment regimens for all patients.

In part three of this thesis I discuss basal cell nevus syndrome (BCNS), a rare genetic disorder based on either a *PTCH1* or a *SUFU* mutation and characterized by multiple BCCs and a broad variety of other symptoms. We developed an up-to-date guideline with emphasis on the value of genetic testing and differences between patients with a *PTCH1* and *SUFU* mutation. We furthermore proposed a diagnostic plan to detect all patients with a germline or postzygotic mutation. The multidisciplinary guideline offers a practical guide for physicians when screening for all possible BCNS symptoms and treatment of BCCs. Treatment with hedgehog pathway inhibitors is shortly addressed in the guideline and more elaborately discussed in an extensive review which was also included in part three. The review provides a clear overview of all available data on treatment with different hedgehog pathway inhibitors in relation to their effectiveness, side effects, improvement of quality of life and tumour recurrence after treatment discontinuation. The guideline and review can be used in daily practice for all patients with BCNS and by physicians that encounter a patient with BCNS.