Journal Reviews

Head & Neck

Long–term follow-up of 44 patients with adenocarcinoma of the nasal cavity and sinuses primarily treated with endoscopic resection followed by radiotherapy

Background: Endoscopic resection followed by radiotherapy as primary treatment for adenocarcinoma of the sinuses is emerging as an alternative to open resection.
Methods: A total of 44 patients primarily treated by an endoscopic approach followed by radiotherapy from 1992 to 2004 seen at our ENT-Department were analysed for outcome and prognostic factors.
Results: Median follow-up was 61 months. Median follow-up of the patients alive at the end of the follow-up period was 100 months. For the 5-year follow-up, the overall survival, disease-specific survival, and recurrence-free survival were 63% (±7% SE), 82% (±6), and 60% (±8%), respectively. The overall survival, disease-specific survival, and recurrence-free survival after 100 months of follow-up were 53% (±8%), 72% (±9%), and 54% (±9%), respectively. Four factors significantly influenced the disease-specific survival.
Conclusion: This study of a homogeneous cohort of patients with sinonasal adenocarcinoma treated by endoscopic resection and radiotherapy confirms that endoscopic resection is a valid alternative to open resection.
Reviewer's opinions: Sino nasal adenocarcinoma is a rare condition. Traditionally been treated by open surgery and post operative radiotherapy. Endoscopic techniques on its own or in combination for the treatment of malignant tumours of nose and sinuses emerged in late 1990s. The advantage is good cosmetic outcome and chance to convert into open if and when appropriate. This is a study looking at 44 previously untreated adenocarinoma of ethmoid (homogeneous group) undergoing endoscopic resection and radiotherapy with long term follow up. The study shows the technique when properly planed and performed by experienced surgeons is an effective alternative to open approaches. – MD
Van Gerven L, Jorissen M, Nuyts S, Hermans R, Vander Poorten V.
Head & Neck • 2011:33(6):898–905.

Neuro-Oncology

A robust model system of paediatric brain tumour cancer stem cells (CSCs)

Recent studies have demonstrated the existence of CSCs in brain tumours that could be the source of tumour resistance and subsequent recurrence. In their paper, Coyle et al characterised CSCs from 7 newly established primary pediatric cell lines, including 2 ependymomas, 2 medulloblastomas, 2 gliomas, and a CNS primitive neuroectodermal tumour. Genomic changes present in the original tumour were retained in culture. In each case, the CSC component was approximately 3–4-fold enriched in neurosphere culture compared with monolayer culture, and a higher capacity for multilineage differentiation was observed for neurosphere-derived cells. Although cells grown as neurospheres showed an altered cell cycle profile, the nestin-expressing cells existed in all phases of the cell cycle, indicating that not all CSCs are quiescent. Furthermore, neurosphere-derived cells demonstrated an increased drug resistance compared with monolayer-derived cells. Those cell lines rapidly formed neurospheres when cultured under appropriate conditions and similarly formed subcutaneous xenografts rapidly in immune-compromised mice, suggesting that the rate of neurosphere formation could be an indicative factor for tumour growth potential. Finally, the authors demonstrated that those orthotopic xenografts were capable of producing a tumour that reflected the gross immunohistological characteristics of their tumour of origin.
Reviewer's opinions: Using 7 primary cell lines representative of a broad range of paediatric brain tumour types, the authors developed a reliable model system that is true to the tumour of origin and representative of that tumour type. Their study enhances our understanding of the biology of CSCs in pediatric brain tumours. This approach could also be applied to other cancer types and used in developing novel anticancer therapies. – QA
Pediatric brain tumour cancer stem cells: cell cycle dynamics, DNA repair, and etoposide extrusion.
Hussein D, Punjaruk W, Storer LC, Shaw L, Ottoman R, Peet A, Miller S, Bandopadhyay G, Heath R, Kumari R, Bowman KJ, Braker P, Rahman R, Jones GD, Watson S, Lowe J, Kerr ID, Grundy RG, Coyle B.
Neuro-Oncology • 2011;13(1):70-83.

Phase IIb study of TGF-β2 inhibitor Trabedersen in glioma treatment

The high-grade gliomas, anaplastic astrocytoma (AA; WHO III) and glioblastoma multiforme (GBM; WHO IV), represent about 60% of all primary malignant brain tumours. Despite current advances in neurosurgery, radio- and chemo-therapy, overall survival is still poor with a median survival of 11.3 months for patients with AA and 7.4 months for patients with GBM. TGF-β2 is overexpressed in more than 90% of high-grade gliomas and its levels are closely related to tumour progression. Trabedersen is a synthetic antisense phosphorothioate oligodeoxy-nucleotide complementary to the mRNA of the human TGF-β2 gene, developed as a targeted therapeutic agent for treating patients with high-grade glioma. The authors carried out a randomised and controlled phase IIb study to evaluate the efficacy and safety of trabedersen administered intratumourally in patients with recurrent/refractory high-grade glioma. One hundred and forty-five patients with GBM or AA were randomly assigned to receive trabedersen at doses of 10 or 80 μM or standard chemotherapy (temozolomide or procarbazine/lomustine/vincristine). Prespecified AA subgroup analysis showed a significant benefit regarding the 14-month tumour control rate for 10 μM trabedersen vs chemotherapy (p=.0032). The 2-year survival rate had a trend for superiority for 10 μM trabedersen vs chemotherapy (p=.10). Exploratory analysis on GBM patients aged ≤55 years with Karnofsky performance status >80% at baseline indicated a 3-fold survival at 2 and 3 years for 10 μM trabedersen vs chemotherapy. The frequency of patients with related or possibly drug-related adverse events was higher with standard chemotherapy (64%) than with 80 μM trabedersen (43%) and 10 μM trabedersen (27%). Their study also suggests 10 μM trabedersen as the optimal dose for further clinical development in high-grade glioma.
Reviewer's opinions: The results from this phase IIb study are encouraging and the authors have demonstrated some degree of efficacy of trabedersen. Moreover, the convection enhanced system employed may have potential in delivering additional biological modifying agents to the whole brain. In this context, while TGF-β2 antisense may modulate immune response, TGF-β1 plays more crucial role in glioma cell invasion and it would be of considerable interest to evaluate similar studies using a TGF-β1antisense approach. – QA
Targeted therapy for high-grade glioma with the TGF-β2 inhibitor trabedersen: results of a randomised and controlled phase IIb study.
Bogdahn U, Hau P, Stockhammer G, Venkataramana NK, Mahapatra AK, Suri A, Balasubramaniam A, Nair S, Oliushine V, Parfenov V, Poverennova I, Zaaroor M, Jachimczak P, Ludwig S, Schmaus S, Heinrichs H, Schlingensiepen KH; Trabedersen Glioma Study Group.
Neuro-Oncology • 2011;13(1):132-42.