Pre-Treatment Corticosteroids on Survival in Head and Neck Cancer Treated with Immune Checkpoint Inhibitors

Parvesh Kumar Jr BA[1], Daniel Uralov MD[1], Sophia Linguiti BA[1], Wesley M. Wride BA[1], Sarah Harrington BA[1], Teresa Duong BS[1], Joseph Curry MD[1]

[1]Department of Head and Neck, Otolaryngology

Background & Objective

- Immune checkpoint inhibitors (ICIs) are now standard in the treatment of advanced Head and Neck Cancer (HNC). Corticosteroids are frequently co-administered for symptom management, treatment-related toxicity, and airway or pain control, but may suppress antitumor T-cell responses critical to ICI efficacy. Whether baseline corticosteroid exposure around ICI initiation is associated with survival outcomes in HNC remains unclear.[1]
- Objective: Determine whether systemic corticosteroid exposure before ICI initiation is associated with overall survival in HNC.[2]

Methods

- Retrospective cohort study using the **TriNetX Global Collaborative Network** (170 healthcare organizations).
- Adult patients with HNC treated with **pembrolizumab, nivolumab, cemiplimab, or durvalumab** were identified.
- Baseline corticosteroid exposure was defined as **systemic prednisone, dexamethasone, methylprednisolone, hydrocortisone, or prednisolone within 3 months before through 1 day after ICI initiation.**
- Exclusions: prior organ transplantation, hematologic malignancy, and immunodeficiency.
- 1:1 propensity score matching was performed using demographics, comorbidities, tobacco use, alcohol-related disorders, and treatment-related variables.
- Pre-match cohorts: no-steroid n = 2,883; steroid n = 2,797.
- Post-match cohorts: no-steroid n = 1,791; steroid n = 1,791.
- Primary outcome: **overall survival up to 5 years.**

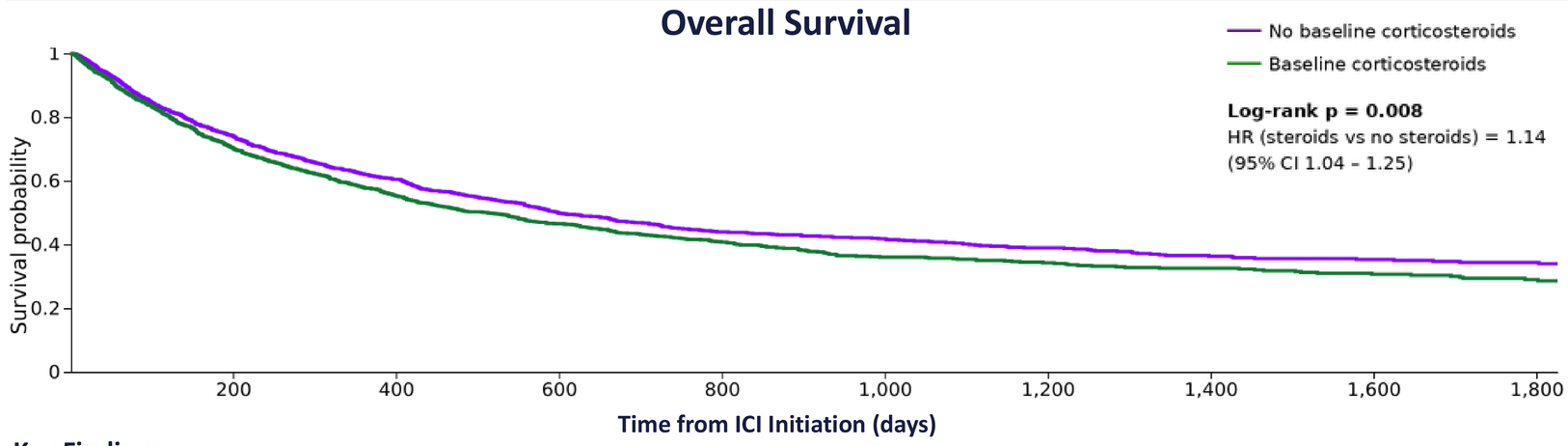
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Results



Key Findings

Outcome	No Baseline Corticosteroids (n = 1,791)	Baseline Corticosteroids (n = 1,791)	Measure of Association
Mortality events, n (%)	807 (45.1%)	864 (48.2%)	—
Median survival, days (95% CI)	599 (336–1,065)	512 (294–924)	—
5-year survival probability	33.96%	28.59%	Absolute difference: 5.37%
Hazard ratio (95% CI)	—	—	1.14 (1.04–1.25), p = 0.008

Baseline corticosteroid exposure near ICI initiation was associated with worse overall survival in HNC

Discussion

- **Biological Plausibility:** Corticosteroids blunt T-Cell activation, deplete low-affinity memory CD8+ T-Cells, and skew CD4+ cells from Th1 to Th2. Thus, lowering ICIs ability to stimulate an immune response.[2,3,4]
- **Conclusion:** Baseline systemic corticosteroid exposure identifies HNC patients with significantly worse survival after ICI initiation (5-year survival: 29% vs 34%; median: 512 vs 599 days). Whether this reflects direct attenuation of ICI efficacy or the clinical indications prompting corticosteroid use requires further study.
- Timing-, dose-, and indication-specific analyses are needed to determine whether particular patterns of corticosteroid exposure are potentially modifiable risk factors for ICI outcomes

Limitations

- Retrospective observational design
- Confounding by indication is the central limitation: patients receiving corticosteroids may have more advanced or symptomatic disease, confounding the observed survival association
- EHR coding and medication capture limitations
- Dose, duration, and reason for corticosteroid use were not fully characterized
- Association does not establish causation

Next Steps

- Investigating why steroids were given, such as airway edema, pain, brain metastases, premedication, COPD, etc.
- Subgroup analysis including oral cavity vs oropharynx vs larynx/hypopharynx, pembrolizumab vs nivolumab vs other ICI, chemotherapy + ICI vs ICI without chemotherapy, radiation vs no radiation
- Timing Sensitivity Analysis 0-7 days → 8-30 days → 31-90 days → no steroid

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