touch™ ONCOLOGY

# What's on the horizon to tackle unmet needs in recurrent/metastatic SCCHN?

**Fact sheet for the treatment of SCCHN**

For more information, visit: www.touchoncology.com

# Unmet treatment needs for patients with R/M SCCHN

**The current standard of care for patients with R/M SCCHN typically comprises immunotherapy and chemotherapy, as monotherapy or in combination, and cetuximab[1,2]**

**As only a minority of patients will respond to ICIs, there is an urgent need to improve antitumour immune responses and expand the treatment options available to patients with R/M SCCHN[3]**

# Future treatment directions: Investigational immunotherapy-based strategies

| | ICIs plus ChT | | ICIs plus cetuximab | | | |
|---|---|---|---|---|---|---|
| **Combination** | **Durvalumab + carboplatin + paclitaxel[4]** | **Pembrolizumab + carboplatin + paclitaxel[5]** | **Pembrolizumab + cetuximab[6]** | **Avelumab + cetuximab[7]** | **Nivolumab + cetuximab[8]** | **Durvalumab + cetuximab[9]** |
| **Study** | Phase II FRAIL-IMMUNE | Phase IV KEYNOTE-B10 | Phase II NCT03082534 | Phase II NCT03494322 | Phase I/II NCT03370276 | Phase II NCT03370276 |
| **Setting** | **First-line** treatment in frail pts with R/M SCCHN not amenable to cisplatin-based ChT N=64 | **First-line** treatment of pts with previously untreated R/M SCCHN N=92 | Platinum-resistant or platinum-ineligible pts with R/M SCCHN N=33 | Pts with R/M SCCHN, no previous treatment with cetuximab N=16 | Second-line and beyond treatment of pts with R/M SCCHN N=45 | Pts with R/M SCCHN N=35 |
| **Key efficacy results** | • **mOS: 18 months**<br>• **24-month OS: 45%**<br>• **mPFS: 7.0 months**<br>• **ORR: 71%**<br>• **mDoR: 5.9 months** | • **mOS: 12.1 months** n=82<br>• **12-month OS: 58%**<br>• **mPFS: 5.6 months**<br>• **ORR: 43%**<br>• **mDoR: 5.5 months** | • **ORR: 45%** | • **ORR: 50%** n=10<br>○ **CR: 20%**<br>○ **PR: 30%** | • **12-month OS: 44%**<br>• **12-month PFS: 19%** | • **mPFS: 5.8 months**<br>• **mOS: 9.6 months**<br>• **ORR: 39% (13/33)**<br>• **mDoR: 8.6 months** |
| **Key safety results** | • **Grade ≥3 AEs: 20.3%** | • **Grade ≥3 AEs: 71%** | • **Serious TRAEs: 15%** | • **Grade 3 AEs: four pts** | • **Grade 4 TRAE: one patient** | • **16 grade 3 TRAEs** |

**PD-1/PD-L1 inhibitors plus carboplatin and paclitaxel demonstrated antitumour activity and tolerable toxicity profiles[4,5]**

**Multiple studies have demonstrated consistent and promising results with PD-1/PD-L1 inhibitors plus cetuximab[10]**

Direct comparisons between trials should not be made due to differences in trial design.

touch™ ONCOLOGY

# Future treatment directions: Novel immunotherapy-based strategies

**Several novel immunotherapy-based strategies have reported clinical activity for R/M SCCHN[11–19]**

| | ICI plus LAG3 inhibitor | Triplet combinations | | ICI plus bispecific antibody |
|---|---|---|---|---|
| **Combination** | **Eftilagimod alpha + pembrolizumab[11]** | **Durvalumab + monalizumab + cetuximab[12]** | **Avelumab + palbociclib + cetuximab[13]** | **BCA101 + pembrolizumab[14]** |
| **Study** | **TACTI-002**<br>Phase II | **NCT02643550**<br>Phase II | **NCT03498378**<br>Phase I | **NCT04429542[15]**<br>Phase I |
| **Setting** | **Second-line** eftilagimod alpha + pembrolizumab (n=37) | **First line**<br>n=40 | **First line**<br>N=12 | **First line**<br>N=33 |
| **Key efficacy results** | • **ORR: 30%**<br>• **mPFS: 2.1 months**<br>• **mOS: 8.7 months** | • **ORR: 33%**<br>• **mPFS: 6.9 months**<br>• **12-month OS: 59%** | • **ORR: 41.7%**<br>• **mPFS: 6.5 months**<br>• **mOS: NR**<br>• **DCR: 75%** | • **ORR: 48%** n=31<br>○ **ORR (HPV-): 65% (13/20)**<br>○ **ORR (CPS 1–19): 50% (5/10)**<br>• **mPFS (HPV-): NR** |
| **Key safety results** | **Most common AEs:**<br>Hypothyroidism (21%)<br>Asthenia (21%)<br>Cough (18%) | **Grade 3 or 4 TRAEs: 48%** | **Any grade TRAEs: 100%**<br>**Grade ≥3 TRAEs: 75%** | **Grade ≥3 TRAEs: 27%** |

## ICI plus TKI

| | Cabozantinib + atezolizumab[16] | Anlotinb + pembrolizumab[17] | Afatinib + pembrolizumab[18] | Lenvatinib + pembrolizumab[19] |
|---|---|---|---|---|
| **Study** | **COSMIC-021**<br>Phase Ib | **NCT04999800**<br>Phase II | **ALPHA study**<br>Phase II | **LEAP-010**<br>**Phase III** |
| **Treatment** | **Second- or third-line** cabozantinib + atezolizumab (N=30) | **First-line**<br>Anlotinb + pembrolizumab (N=15) | **Second-line**<br>Afatinib + pembrolizumab (n=29) | **First-line**<br>**Lenvatinib + pembrolizumab** (n=256) or placebo + pembrolizumab (n=255) |
| **Key efficacy results** | • **ORR: 17%**<br>• **mPFS: 2.9 months**<br>• **mOS: 9.2 months** | • **ORR: 46.7%**<br>• **mPFS: NR**<br>• **mOS: NR** | • **mPFS: 4.1 months**<br>• **mOS: 8.9 months** | • **ORR: 46.1% vs 25.4%***<br>• **mPFS: 6.2 vs 2.8 months***<br>• **mOS: 15.0 vs 17.9 months*** |
| **Key safety results** | **Most common TRAEs:**<br>Fatigue (30%)<br>Stomatitis (30%)<br>Hypertension (27%) | **Most common TRAEs:**<br>Hypertension (25%) | **Most common TRAEs:**<br>Skin rash (75.9%)<br>Diarrhoea (58.9%)<br>Paronychia (44.8%) | **Grade ≥3 TRAEs (IA2):**<br>61.4% vs 17.8% |

### CTLA-4

**Multiple studies did not meet their primary end point (OS/ORR) when assessing the efficacy of CTLA-4 inhibition in combination with anti-PD-1/PD-L1 monoclonal antibodies compared to SoC regimens[20–23]**

Direct comparisons between trials should not be made due to differences in trial design.

*Per the prespecified analysis plan, ORR and PFS are reported from the first interim analysis (IA1) and OS is reported from second interim analysis (IA2). Data cutoff dates were July 6, 2022 for IA1 and May 30, 2023 for IA2.

touch ONCOLOGY

# Future treatment directions: Targeted therapies

| | Targeting VEGF | | | | ADCs | | |
|---|---|---|---|---|---|---|---|
| **Treatment** | **Bevacizumab** | | | | **Tisotumab vedotin[29]** | **Enfortumab vedotin[30]** | **MRG003[31]** |
| **Study** | Phase II[24] Previously untreated R/M SCCHN N=40 | Phase III (E1305)[25] Chemotherapy naive R/M SCCHN N=403 | Phase II[26] R/M SCCHN with no more than one prior treatment N=46 | Phase II[27] n=48 | Phase II innovaTV 207 | Phase II EV-202 | Phase II[32] NCT04868162 |
| **Setting** | Pemetrexed + bevacizumab | **Platinum doublet ChT + bevacizumab** vs platinum doublet ChT | Cetuximab + bevacizumab | Erlotinib + bevacizumab | Pts with R/M SCCHN who have received prior lines of therapy including platinum therapy (93% had received an ICI) (n=15) | Pts with la/m HNC who have previously received one platinum-based therapy (n=46) | Pts with R/M SCCHN who had progressed on at least one line of standard therapy (N=67) |
| **Key efficacy results** | • **mOS: 11.3 months**<br>• **ORR: 30%** | • **mOS: 12.6** vs 11.0 months<br>• **mPFS: 6.0** vs 4.3 months<br>• **ORR: 35.5%** vs 24.5% | • **mOS: 7.5 months**<br>• **mPFS: 2.8 months**<br>• **ORR: 16%** | • **mOS: 7.1 months**<br>• **mPFS: 4.1 months** | • **ORR: 40%** | • **ORR: 23.9%**<br>• **mPFS: 3.94 months**<br>• **mOS: 5.98 months** | • **ORR (EGFR+): 30.6%**<br>• **ORR:* 43%**<br>• **mPFS: 4.2 months**<br>• **mOS: 11.3 months** |
| **Key safety results** | **Grade 3 to 5 bleeding events: 15%** | **Treatment-related grade 3 to 5 bleeding events: 6.7%** vs 0.5% | **Grade 3 or 4 AE: <10%** | **Most common AE of any grade:**<br>• **Rash and diarrhoea** | **TRAEs: 13 pts**<br>• **Asthenia (n=7)**<br>• **PSN (n=7)**<br>• **Vomiting (n=5)** | **TRAEs of special interest:**<br>• **Skin reactions (45.7%)**<br>• **Peripheral neuropathy (32.6%)**<br>• **Hyperglycaemia (4.3%)** | **Common TRAEs:**<br>• **Constipation (25.8%)**<br>• **Pruritus (24.2%)**<br>• **Anaemia (22.6%)** |

**The VEGF pathway is a promising therapeutic target in SCCHN; however, further studies should focus on minimizing unwanted adverse effects, especially bleeding events[28]**

**ADCs have shown promising efficacy and manageable safety profiles in various phase II trials for the treatment of R/M SCCHN[29–31]**

*In second- and third-line patients who had previously failed prior platinum and PD-1/PD-L1 inhibitor and who had received 2.3 mg/kg dose of MRG003.
Direct comparisons between trials should not be made due to differences in trial design.

touch™ ONCOLOGY

# Future treatment directions: Targeted therapies

| | HRAS inhibitor | PI3K inhibition | |
|---|---|---|---|
| **Treatment** | **Tipifarnib**[33] | **Buparlisib + cetuximab**[34] | **Buparlisib + paclitaxel** vs placebo + paclitaxel[35] |
| **Study** | Phase II<br>NCT03719690<br>N=59 | Phase Ib<br>NCT01816984<br>(N=12) | Phase II<br>BERIL-1<br>(n=158) |
| **Key efficacy results** | • **ORR: 30%** (n=50; investigator assessment)<br>• **mOS: 7.0 months** | • **PR: 1 patient** n=10<br>• **SD: 4 pts** | • **ORR: 39%** vs 14%<br>• **mOS: 10.0** vs 6.5 months |
| **Key safety results** | **Grade ≥3 TRAEs: 56%**<br>• **Neutropenia (24%)**<br>• **Anaemia (20%)**<br>• **Leukopenia (14%)**<br>• **Febrile neutropenia (7%)** | **Grade ≥3 AEs: 10 pts** | **Grade 3 or 4 AEs:**<br>• **Hyperglycaemia (22%** vs 3%)<br>• **Anaemia (18%** vs 12%)<br>• **Neutropenia (17%** vs 5%)<br>• **Fatigue (8%** vs 10%) |

**Tipifarnib showed antitumor activity for patients with mutated *HRAS* SCCHN post-IO and as later-line therapy**[33]

**Clinical evaluation of PI3K inhibitors in SCCHN is mainly in early phase clinical trials**[28]

## EGFR inhibition

**Cetuximab**

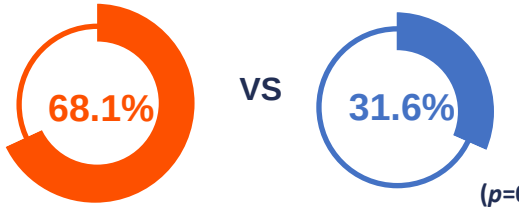
- **The only EGFR-targeted therapy currently approved in Europe, the USA and Japan for SCCHN**[36–38]

**Other EGFR mAbs/inhibitors of interest in SCCHN include panitumumab, gefitinib, afatinib, dacomitinib, nimotuzumab, lapatinib and poziotinib**[28]

**However, only 5% of HNC patients have EGFR alterations, which may contribute to the limited effectiveness of EGFR TKIs**[28]

## EGFR expression and HPV status

- **Overexpression of EGFR was observed more frequently in HPV- tumours than in HPV+ tumours**[39]




- **Recent studies have shown inferior outcomes in patients with HPV+ SCCHN who received cetuximab in combination with RT or cisplatin**[40]

Direct comparisons between trials should not be made due to differences in trial design.

touch ONCOLOGY

# Abbreviations and references

## Abbreviations

ADC, antibody–drug conjugate; AE, adverse event; ChT, chemotherapy; CPS, combined positive score; CR, complete response; CTLA-4, cytotoxic T-lymphocyte associated protein 4; DCR, disease control rate; DoR, duration of response; EGFR, epidermal growth factor receptor; HNC, head and neck cancer; HPV, human papillomavirus; HRAS, Harvey rat sarcoma viral oncogene homolog; ICI, immune checkpoint inhibitor; LAG3, lymphocyte activation gene 3; la/m, locally advanced or metastatic; mAb, monoclonal antibody; m, median; NR, not reached; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PI3K, phosphatidylinositol 3-kinase; PR, partial response; PSN, peripheral sensory neuropathy; pts, patients; R/M, recurrent or metastatic; RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck; SD, stable disease; SoC, standard of care; TKI, tyrosine kinase inhibitor; TRAE, treatment-related AE; VEGF, vascular endothelial growth factor.

## References


1. Machiels JP, et al. *Ann Oncol.* 2020;31:1462–75.
2. NCCN. Head and neck cancers. V2.2024. Available at: www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf (accessed January 2024);
3. Borcoman E, et al. *Cancers.* 2021;13. doi: 10.3390/cancers13112573.
4. Fayette J, et al. *J Clin Oncol*. 2023;41(Suppl. 16):Abstr 6003.
5. Dzienis MR, et al. *Ann Oncol.* 2022;33(Suppl. 7):S839–40.
6. Sacco AG, et al. *Lancet Oncol.* 2021;22:883–92.
7. Forster M, et al. *Ann Oncol.* 2020;31(Suppl. 4):S665
8. Chung CH, et al. *Cancers (Basel).* 2021;13:1180.
9. Gulati S, et al. *Clin Cancer Res*. 2023;29:1906–15.
10. Wise-Draper TM, et al. Am Soc Clin Oncol Educ Book. 2022;42:1–14.
11. Doger de Spéville BD, et al. J Clin Oncol. 2023;41(Suppl. 16):6029.
12. Colevas DA, et al. *Ann Oncol.* 2021;32(Suppl. 7):S1432.
13. Dennis MJ, et al. *Oral Oncol.* 2022;135:106219.
14. Hanna GJ, et al. *Ann of Oncol.* 2023;34:S582–3.
15. ClinicalTrials.gov. NCT04429542. Available at: https://clinicaltrials.gov/NCT04429542 (accessed January 2024).
16. Rottey S, et al. *J Immunother Cancer.* 2022;10(Suppl. 2): A597.
17. Gui L, et al. *Ann Oncol.* 2022;33(Suppl. 9):S1524.
18. Kao HF, et al. *Clin Cancer Res.* 2022;128:1560–71.
19. Licitra L, et al. Presented at: Multidisciplinary Head and Neck Cancers Symposium 2024, Phoenix, AZ, USA. 29 February–2 March 2024. Abstract.
20. Ferris RL, et al. *Ann Oncol.* 2020;31:942–50.
21. Psyrri A, et al. *Ann Oncol.* 2023;34:262–74.
22. Harrington KJ, et al. *JAMA Oncol.* 2023;9:779–89.
23. Haddad RI, et al. *J Clin Oncol.* 2022;41:2166–80
24. Argiris A, et al. *J Clin Oncol.* 2011;29:1140–5;
25. Argiris A, et al. *J Clin Oncol*. 2019;37:3266–74
26. Argiris A, et al. *Ann Oncol.* 2013;24:220–5.
27. Cohen E, et al. *Lancet Oncol.* 2009;10:247–57.
28. Li Q, et al. Signal *Transduct Target Ther.* 2023;8:31.
29. Cirauqui B, et al. *Cancer res.* 2023;83 (Suppl. 8):CT164.
30. Swiecicki P, et al. *J Clin Oncol.* 2023;41:6017.
31. Xue L, et al. *Ann Oncol.* 2023; 34(Suppl. 2):S554–94
32. ClinicalTrials.gov. NCT04868162. Available at: https://clinicaltrials.gov/NCT04868162 (accessed January 2024).
33. Ho AL, et al. *Ann Oncol.* 2023;34:S1286–87.
34. Brisson RJ, et al. *Head Neck.* 2019;41:3842–49.
35. Soulieres D, et al. *J Clin Oncol.* 2016;34:6008.
36. EMA. Cetuximab SmPC. Available at: https://bit.ly/4b14A9Q (accessed January 2024).
37. FDA. Cetuximab PI. Available at: https://bit.ly/47Oulrq (accessed January 2024).
38. Szturz P, et al. J *Clin Oncol.* 2017;35:2229–31.
39. Chen Y, et al. *Int Immunopharmacol.* 2023:120:110329.
40. Alsahafi EN, et al. *Cancer Lett.* 2021:498:80–97.




touch™ ONCOLOGY