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Oncology and surgery

Dra. Leyre Aguado Gil

Scientific Initiative of:

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UPDATES IN MERKEL CELL CARCINOMA THERAPIES

- Immunotherapy in Merkel cell carcinoma:
  - Avelumab (anti PD-L1) approved April 2017
  - Pembrolizumab (anti PD-1) approved December 2018

J Clin Oncol. 2019 Feb 6:JCO1801896. doi: 10.1200/JCO.18.01896. [Epub ahead of print]

Durable Tumor Regression and Overall Survival in Patients With Advanced Merkel Cell Carcinoma Receiving Pembrolizumab as First-Line Therapy.

Nghiem P[1], Bhatia S[1], Lipson EJ[2], Sharfman WH[2], Kudchadkar RR[3], Brohl AS[4], Friedlander PA[5], Daud A[6], Kluger HM[7], Reddy SA[8], Boulmay BC[9], Riker AI[9], Burgess MA[10], Hanks BA[11], Olencki T[12], Margolin K[13], Lundgren LM[14], Soni A[2], Ramchurren N[14], Church C[15], Park SY[15], Shinohara MM[15], Salim B[16], Taube JM[2], Bird SR[17], Ibrahim N[17], Fling SP[14], Homet Moreno B[17], Sharon E[18], Cheever MA[14], Topalian SL[2].

UPDATES IN MERKEL CELL CARCINOMA THERAPIES

PD-1 /PD-L1 blockade superior to chemotherapy

	Avelumab	Avelumab	Pembrolizumab	Nivolumab (off label use)	Chemotherapy	Chemotherapy
Patients	88	29	50	22	62	30
Timing of therapy	≥2nd line	1st line	1st line	1st and 2nd line	1st line	2nd line
Type of study	Phase 2	Phase 2	Phase 2	Phase 2	retrospective	retrospective
Overall Response Rate	**33% (CI 23-44)**	**62% (CI 42-79)**	**56% (CI 35-76)**	**68% (CI 45-86)**	**55%**	**23%**
Complete response	11%	14%	24%	14%	13%	3%
Partial response	22%	48%	32%	55%	42%	20%
Median duration of response (mo)	Not reached (CI 18-NE)	Not estimable	Not reached (RG 5.9-34.5+)	Not reported	2.8 (RG 0.4-30.9)	3.3 (RG 0.2-7.4)

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- *Nghiem P et al. Durable Tumor Regression and Overall Survival in Patients With Advanced Merkel Cell Carcinoma Receiving Pembrolizumab as First-Line Therapy. J Clin Oncol. 2019 Feb 6:JCO1801896*

- *Topalian et al. Abstract CT074: Non-comparative, open-label, multiple cohort, phase 1/2 study to evaluate nivolumab (NIVO) in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in Merkel cell carcinoma (MCC). Cancer Res July 1 2017 (77) (13 Supplement) CT074; **DOI:**10.1158/1538-7445.AM2017-CT074*

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CUTANEOUS T-CELL LYMPHOMA

Lancet Oncol. 2018 Sep;19(9):1192-1204. doi: 10.1016/S1470-2045(18)30379-6. Epub 2018 Aug 9.

Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial.

Kim YH[1], Bagot M[2], Pinter-Brown L[3], Rook AH[4], Porcu P[5], Horwitz SM[6], Whittaker S[7], Tokura Y[8], Vermeer M[9], Zinzani PL[10], Sokol L[11], Morris S[7], Kim EJ[4], Ortiz-Romero PL[12], Eradat H[13], Scarisbrick J[14], Tsianakas A[15], Elmets C[16], Dalle S[17], Fisher DC[18], Halwani A[19], Poligone B[20], Greer J[21], Fierro MT[22], Khot A[23], Moskowitz AJ[6], Musiek A[24], Shustov A[25], Pro B[26], Geskin LJ[27], Dwyer K[28], Moriya J[28], Leoni M[28], Humphrey JS[28], Hudgens S[29], Grebennik DO[28], Tobinai K[30], Duvic M[31]; MAVORIC Investigators.

⊕ Collaborators (47)

⊕ Author information

Erratum in

Correction to Lancet Oncol 2018; 19: 1192-204. [Lancet Oncol. 2018]

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CUTANEOUS T-CELL LYMPHOMA

- Mogamulizumab:
  - monoclonal antibody
  - selectively binds to C-C chemokine receptor 4 (CCR4)
- Open-label, international, randomized trial
- 372 patients with relapsed or refractory mycosis fungoides or Sézary syndrome
  - at least one previous systemic therapy

CUTANEOUS T-CELL LYMPHOMA

- Overall response:
  - Mogamulizumab 28% vs Vorinostat 5%

- Response to Mogamulizumab
  - Mycosis fungoides: 21% vs Sézary syndrome: 37%
  - Skin 42%, blood 68%, lymph nodes 17%, viscera 0%
  - No correlation with tissue/blood CCR4 expression

CUTANEOUS T-CELL LYMPHOMA

- Most common adverse events with mogamulizumab
  - Infusion reaction (30%)
  - Fatigue, diarrhea, infection, dermatitis (20-25%)

Cutaneous T-cell lymphoma

- CCR4 is highly expressed on both malignant and regulatory T cells.
  - Depletion of regulatory T cells following mogamulizumab
    - Augment antitumor response but also potentiate graft-vs-host disease (GVHD).
- Short interval (<50 days) between mogamulizumab and allo stem cell transplant: greater risk (28-50%) of severe acute GVHD

JAMA Dermatol. 2018 Jun 1;154(6):728-730. doi: 10.1001/jamadermatol.2018.0884.

Potential Association of Anti-CCR4 Antibody Mogamulizumab and Graft-vs-Host Disease in Patients With Mycosis Fungoides and Sézary Syndrome.

Dai J[1], Almazan TH[1], Hong EK[1], Khodadoust MS[2], Arai S[3], Weng WK[1,3], Kim YH[1].

J Clin Oncol. 2016 Oct 1;34(28):3426-33. doi: 10.1200/JCO.2016.67.8250. Epub 2016 Aug 9.

Pretransplantation Anti-CCR4 Antibody Mogamulizumab Against Adult T-Cell Leukemia/Lymphoma Is Associated With Significantly Increased Risks of Severe and Corticosteroid-Refractory Graft-Versus-Host Disease, Nonrelapse Mortality, and Overall Mortality.

Fuji S[1], Inoue Y[2], Utsunomiya A[2], Moriuchi Y[2], Uchimaru K[2], Choi I[2], Otsuka E[2], Henzan H[2], Kato K[2], Tomoyose T[2], Yamamoto H[2], Kurosawa S[2], Matsuoka K[2], Yamaguchi T[2], Fukuda T[2].

BASAL CELL CARCINOMAS

- New topical HH inhibitor: Patidegib
  - Phase 2:
    - Reduces BCC diameter
    - Fewer new BCC
    - Correlation of tumor response and biomarker (GLU1 mRNA)
    - Minimal systemic exposure
  - Now phase 3 trial