3

REAL-WORLD EFFICACY OF IMMUNOTHERAPY IN PATIENTS WITH ACRAL MELANOMA IN SPAIN: RESULTS FROM THE GEM1801 STUDY

Maria Gonzalez-Cao [1]*, Miguel-Ángel Berciano-Guerrero [2], Eva Muñoz-Couselo [3], José Luis Manzano [4], Pablo Cerezuela-Fuentes [5], Guillermo Crespo [6], Ainara Soria [7], Pablo Ayala de Miguel [8], Lourdes Gutiérrez Sanz [9], Carlos Aguado de la Rosa [10], Almudena García Castaño [11], Teresa Puértolas [12], Enrique Espinosa [13], Javier Medina [14], Lorena Bellido [15], Alfonso Berrocal [16], Margarita Majem [17], Rafael López Castro [18], Salvador Martín Algarra [19], Iván Márquez-Rodas [20]

[1] *Medical Oncology Department. Instituto Oncologico Dr Rosell, Dexeus University Hospital,Barcelona, Spain*

[2] *Medical Oncology Department. Hospital Regional Universitario de Málaga (HRU). Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Málaga, Spain.*

[3] *Medical Oncology Department. Hospital Universitari Vall d'Hebron y Vall D'hebron Institute of Oncology (VHIO), Barcelona, Spain.*

[4] *Medical Oncology Department. Instituto Catalán de Oncología, ICO-Badalona, H. Germans Triasi Pujol, Badalona, Spain.*

[5] *Medical Oncology Department. Hospital Clínico Universitario Virgen de la Arrixaca, Instituto Murciano de Investigación Biosanitaria (IMIB)-Arrixaca, Ciudad de Murcia, Spain.*

[6] *Medical Oncology Department. Hospital Universitario de Burgos, Burgos, Spain.*

[7] *Medical Oncology Department. Hospital Universitario Ramón y Cajal, Madrid, Spain.*

[8] *Medical Oncology Department. Hospital Universitario San Pedro de Alcántara, Cáceres, Spain.*

[9] *Medical Oncology Department. Hospital Universitario Puerta de Hierro, Madrid, Spain.*

[10] *Medical Oncology Department. Hospital Universitario Clínico San Carlos, Madrid, Spain.*

[11] *Medical Oncology Department. Hospital Universitario Marqués de Valdecilla, Santander, Spain.*

[12] *Medical Oncology Department. Hospital Universitario Miguel Servet, Zaragoza, Spain.*

[13] *Medical Oncology Department. Hospital Universitario La Paz, CIBERONC, Madrid, Spain.*

[14] *Medical Oncology Department. Hospital Universitario Toledo, Toledo, Spain.*

[15] *Medical Oncology Department. Complejo Asistencial Universitario de Salamanca. Instituto de Investigación Biomédica de Salamanca (IBSAL) Salamanca, Spain.*

[16] *Medical Oncology Department. Hospital General Universitario Valencia, Valencia, Spain.*

[17] *Medical Oncology Department. Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*

[18] *Medical Oncology Department. Hospital Clínico Universitario de Valladolid, Valladolid, Spain.*

[19] *Medical Oncology Department. Clínica Universidad de Navarra, Pamplona, Spain.*

[20] *Medical Oncology Department. Hospital General Universitario Gregorio Marañón, Madrid, Spain.*

Corresponding Author: Maria Gonzalez-Cao Maria Gonzalez mgonzalezcao@oncorosell.com

Background: Acral melanoma (AM) is uncommon in non-Asian race. Poor response to immunotherapy compared to cutaneous melanoma (CM) has been reported, though most studies have been performed in Asian populations.

Method: We analyzed the clinical outcomes of stage III and stage IV AM and CM patients registered in the nationwide Spanish Melanoma Group Registry (GEM 1801). The impact of immunotherapy was compared between AM and CM in terms of relapse-free survival (RFS), response rate (ORR), progression-free survival (PFS), and overall survival (OS). A multivariable Cox regression analysis was performed to adjust for potential confounders

Results: The register included 69 AM (17 stage III and 52 stage IV) and 729 CM (191 stage III and 538 stage IV) cases. Most common location of AM was on soles (n=51), followed by nails (n=16) and palms (n=1). Patients were non-Hispanic white, except for two IV AM patients (one Asian and one Hispanic white) and one Hispanic White patient stage III AM. AM cases had deeper melanomas than CM in the stage III cohort (T4b in 52.9% for AM vs. 25.1% for CM, p<0.01), while in the stage IV cohort significant differences were observed only for age (median age 73 for AM vs. 66 years for CM, p=0.0015). No significant differences were found in other baseline characteristics between AM and CM. In the adjuvant setting, 13 AM and 156 CM patients were treated with immunotherapy. Median relapse free survival (RFS) was 15.35 months (95% CI 9.97-NR) versus NR (55.8-NR) (p =0.018) and five-year overall survival (OS_{5y}) was 36.2% vs. 78.57% (p= 0.0266), for AM and CM, respectively. Regarding stage IV, 49 AM and 316 CM patients received immunotherapy as first line (most anti-PD-1 as single agent, while 12% AM and 13% CM received nivolumab plus ipilimumab). Response rate was 12% versus 40% (p=0.0033), median progression free survival (PFS) was 5.5 months (95% CI 3.97-8.23) versus 15.35 months (95% CI 8.97- 26.3) (p=0.001)
and median OS was 17.33 months (95% CI 13.32-39.97) versus 43.0 months (95%CI 30.81 , NR) (p=0.007) for AM and CM respectively (Table 1). After adjusting for potential confounders, AM remained associated with higher risk of progression (HR 0.53; 95% CI: 0.34–0.83; *p* = 0.005).

Conclusions: Our data confirms a poor outcome of AM in Spanish population. Tailored treatment strategies should be developed in AM.

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Trial registration clinicaltrials.gov: NCT03605771

Table 1. Main results

Endpoint	AM	CM	*p-value*
Stage III			
Median RFS; m (95% CI)	15.4 (9.97-NR)	NR (55.8-NR)	0.018
3-y RFS; % (95% CI)	0 (NA)	71.8 (63.2-81.6)	
5-y OS; % (95% CI)	36.2 (8.7-100)	78.6 (68.3-90.4)	0.027
Stage IV			
ORR; %	15	39	0.0033
Median PFS; m (95%CI)	5.5 (3.97-8.23)	15.35 (8.97- 26.3)	0.001
5-y PFS; % (95% CI)	10.6 (3.4- 32.8)	34.7 (28.4-42.3)	
Median OS; m (95%CI)	17.3 (13.3-40)	43.0 (30.8-NR)	0.007
5-y OS; % (95% CI)	18.5 (8.2-42.1)	43.6 (36.1-52.6)	