

# **Nivolumab nel carcinoma renale metastatico: esperienza italiana**

**Ugo De Giorgi**

Istituto Tumori Romagna IRST IRCCS Meldola

on behalf of the Italian EAP RCC Group

# Real world data from the Italian expanded access program (EAP): updated safety and efficacy results of nivolumab for metastatic renal cell carcinoma

*Ugo De Giorgi, Giacomo Carteni, Umberto Basso, Luca Galli, Simone Scagnoli, Claudia Caserta, Sandro Pignata, Annalisa Guida, Alessandra Bearz, Sebastiano Buti, Giovanni Lo Re, Alfredo Berruti, Alketa Hamzaj, Francesco Cognetti, Francesca Rastelli, Azzurra Damiani, Camillo Porta, Tania Losanno, Daniele Turci, Giuseppe Procopio; the Italian EAP RCC Group*

*<sup>1</sup>Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; <sup>2</sup>AORN A. Cardarelli, Napoli, Italy; <sup>3</sup>Istituto Oncologico Veneto, Padova, Italy; <sup>4</sup>AOU Pisana Spedali Riuniti di S. Chiara, Pisa, Italy; <sup>5</sup>Policlinico Umberto I, Roma, Italy; <sup>6</sup>AO Santa Maria, Terni, Italy; <sup>7</sup>Istituto Pascale, Napoli, Italy; <sup>8</sup>AOU di Modena, Modena, Italy; <sup>9</sup>Istituto Nazionale Tumori, Aviano, Italy; <sup>10</sup>AOU di Parma, Parma, Italy; <sup>11</sup>AO Santa Maria degli Angeli, Pordenone, Italy; <sup>12</sup>ASST Spedali Civili di Brescia, Brescia, Italy; <sup>13</sup>Azienda USL 8, Arezzo, Italy; <sup>14</sup>IFO Regina Elena, Roma, Italy; <sup>15</sup>UOC Oncologia Fermo Area Vasta 4, Fermo, Italy; <sup>16</sup>Ospedale San Martino IST Genova, Genova, Italy; <sup>17</sup>IRCCS San Matteo, Pavia, Italy; <sup>18</sup>San Camillo Forlanini, Roma, Italy; <sup>19</sup>Ospedale Santa Maria delle Croci, Ravenna, Italy; <sup>20</sup>Istituto Nazionale Tumori, Milano, Italy*

# Expanded Access Named Patient Program

## KEY INCLUSION CRITERIA:

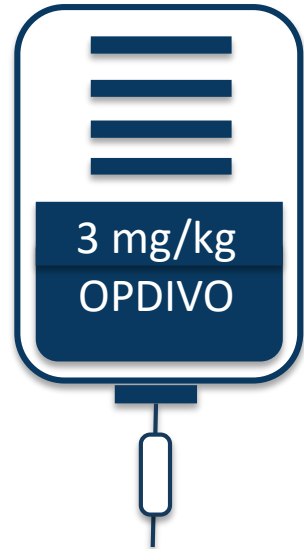
- Patients with histologically confirmed advanced or metastatic RCC
- Must have received at least 1 prior therapy regimens in the advanced or metastatic setting.
- Karnofsky Performance Score (KPS)  $\geq$  70%
- Patients are eligible if CNS metastases are adequately treated and patients are neurologically returned to baseline for at least 2 weeks prior to first dose of program medication. In addition, patients must be either off corticosteroids, or on a stable or decreasing dose of  $\leq$  10 mg daily prednisone (or equivalent) for at least 2 weeks prior to first dose of program medication.

## KEY EXCLUSION CRITERIA:

- Patients with untreated CNS metastases are excluded
- Patients with an active, known or suspected autoimmune disease.
- Patients with a condition requiring systemic treatment with either corticosteroids ( $>$  10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of first program dose.
- Prior treatment with an anti-PD-1, anti-PD-L1, anti PD L2, anti-CD137, or anti CTLA 4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways.

## TREATMENT REGIMEN AND SCHEDULE:


- The dose and schedule of nivolumab is 3 mg/kg IV every 2 weeks
- Patients treated to a maximum of 24 months
- For patients treated with nivolumab it is permitted to continue treatment beyond initial progressive disease as long as they meet predefined criteria




# EAP Baseline Characteristics

## Nivolumab (n = 389)

Median age, years (range)	65 (34, 85)
≥70 years, n (%)	125 (32)
≥75 years, n (%)	70 (18)
Male, n (%)	291 (75)
Female, n (%)	98 (25)
ECOG PS, n (%)	
0	176 (47)
1	174 (47)
2	24 (6)
NA	15
Number of prior systemic regimens, %	
1	80 (21)
2	136 (35)
3	101 (26)
≥4	69 (18)
NA	3



In total, 389  
Italian patients  
received at least  
one dose of  
nivolumab in EAP  
across 108 sites



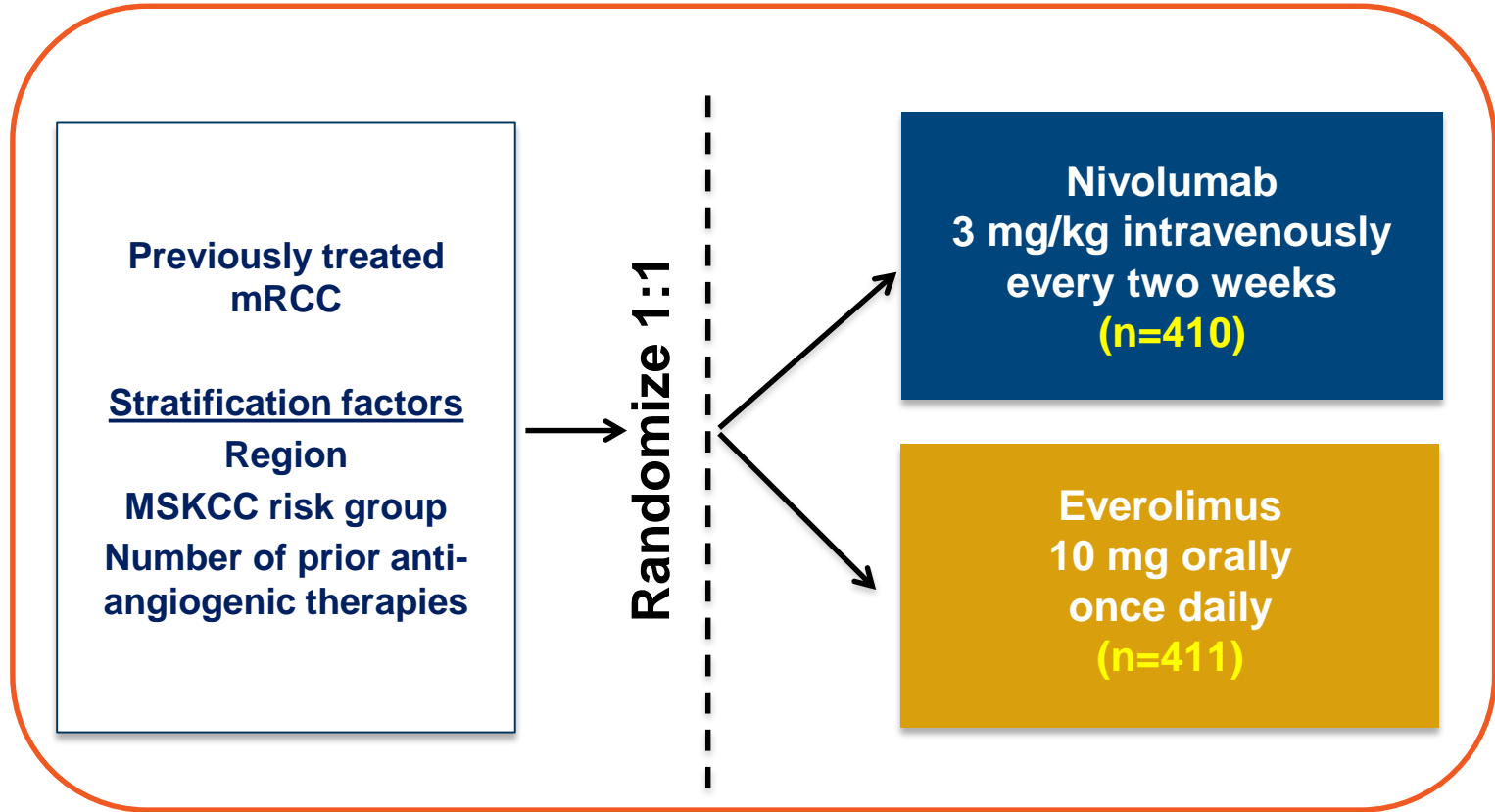
# EAP Baseline Characteristics

Nivolumab (n = 389)	
<b>Histology</b>	
Clear cell	346 (92)
Non-clear cell	32 (8)
NA	11
<b>Metastatic sites, n (%)</b>	
Bone	193 (50)
Nodes	238 (61)
Brain	32 (8)
Liver	128 (33)
Lung	286 (73)



In total, 389 Italian patients received at least one dose of nivolumab in EAP across 108 sites

# CheckMate 025 Study Design



## Checkmate 025 Baseline Characteristics

	Nivolumab N = 410	Everolimus N = 411
Median age (range), years	62 (23–88)	62 (18–86)
Sex, %		
Female	23	26
Male	77	74
MSKCC risk group, %		
Favorable	35	36
Intermediate	49	49
Poor	16	15
Number of prior anti-angiogenic regimens in advanced setting, %		
1	72	71
2	28	29
Region, %		
US/Canada	42	42
Western Europe	34	34
Rest of the world	23	24

Subgroup	Nivolumab n/N	Everolimus n/N
<b>MSKCC risk group</b>		
Favorable	45/145	52/148
Intermediate	101/201	116/203
Poor	37/64	47/60
<b>Prior anti-angiogenic regimens</b>		
1	128/294	158/297
2	55/116	57/114
<b>Region</b>		
US/Canada	66/174	87/172
Western Europe	78/140	84/141
Rest of the world	39/96	44/98
<b>Age, years</b>		
<65	111/257	118/240
≥65 to <75	53/119	77/111
≥75	19/34	19/34
<b>Sex</b>		
Female	48/95	56/107
Male	135/315	159/304

**Table 1. Baseline Demographic and Clinical Characteristics of the Patients Who Underwent Randomization.**

Characteristic	Nivolumab Group (N = 410)	Everolimus Group (N = 411)	Total (N = 821)
Karnofsky performance status — no. (%)‡			
<70	2 (<1)	1 (<1)	3 (<1)
70	22 (5)	30 (7)	52 (6)
80	110 (27)	116 (28)	226 (28)
90	150 (37)	130 (32)	280 (34)
100	126 (31)	134 (33)	260 (32)
Disease sites that could be evaluated — no. (%)			
1	68 (17)	71 (17)	139 (17)
≥2	341 (83)	338 (82)	679 (83)
Site of metastasis — no. (%)			
Lung	278 (68)	273 (66)	551 (67)
Liver	100 (24)	87 (21)	187 (23)
Bone	76 (19)	103 (25)	179 (22)
Previous nephrectomy — no. (%)			
Yes	364 (89)	339 (83)	703 (86)
No	46 (11)	52 (13)	98 (12)

- No accepted brain metastases
- Clear cell only

# Patient disposition

Disposition	N = 389
Discontinued treatment, n (%)	231 (59)
Reason for discontinuation, n/n (%)	
Progressive disease	172/231 (76)
Death	19/231 (8)
AEs or serious AEs	18*/231 (8)
Treatment-related AEs	9/231 (4)
Other	19/231 (8)

\*18 (8%) of 231 patients discontinued nivolumab treatment for toxicity reasons; these were considered to be **drug related in 9 (4%)** of 231 patients and included liver toxicity, hypothyroidism, hyperglycemia, diarrhea, hypertension, skin toxicity, tremor, ptosis, and bronchiolitis obliterans organizing pneumonia (BOOP)

# Patient disposition

Disposition	N = 389
<b>Discontinued treatment, n (%)</b>	231 (59)
<b>Reason for discontinuation, n/n (%)</b>	
Progressive disease	172/231 (76)
Death	19/231 (8)
AEs or serious AEs	18*/231 (8)
Treatment-related AEs	9/231 (4)
Other	19/231 (8)

Checkmate 025 rate of discontinuation

	Nivolumab N = 406		Everolimus N = 397	
	Any Grade	Grade 3-4	Any Grade	Grade 3-4
<b>Treatment-related AEs, %</b>	79	19	88	37
<b>Treatment-related AEs leading to discontinuation, %</b>	8	5	13	7
<b>Treatment-related deaths, n</b>	0		2 <sup>a</sup>	

# Response to treatment

Characteristic	N = 389
<b>ORR, n (%)</b>	86/389 (22)
95% CI (%)	18, 26
<b>Best objective response, n (%)</b>	
Complete response	2 (<1)
<b>Partial response</b>	<b>84 (22)</b>
Stable disease	120 (31)
Progressive disease	144 (37)
Not determined	39 (10)

- ORR was 22%
  - 100 (26%) patients were treated beyond progression
- 25 patients treated beyond progression obtained a subsequent benefit (6 had a partial response and 19 had stable disease)

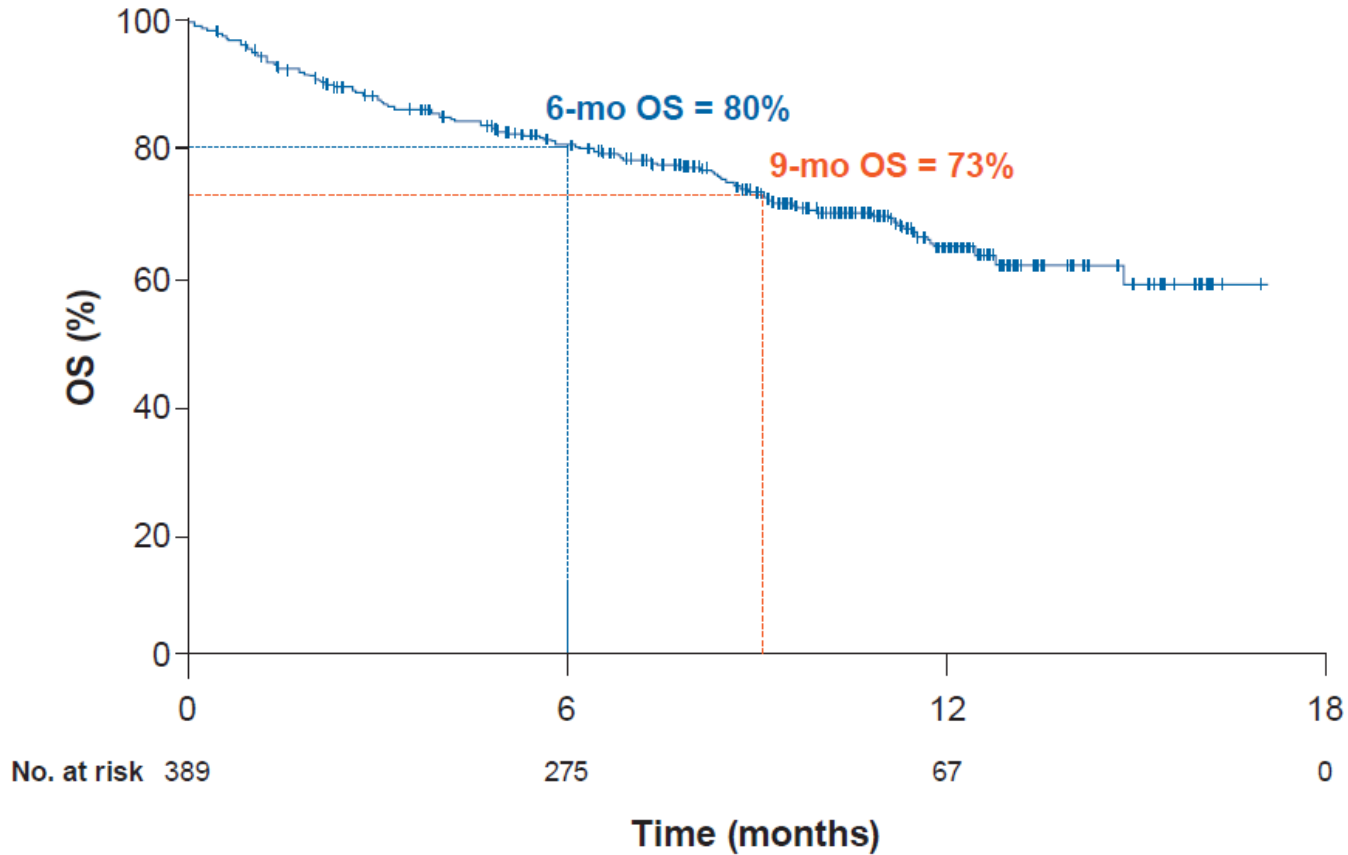
# Response to treatment

Characteristic	N = 389
<b>ORR, n (%)</b> 95% CI (%)	86/389 (22)18,26
<b>Best objective response, n (%)</b>	
Complete response	2 (<1)
<b>Partial response</b>	<b>84 (22)</b>
Stable disease	120 (31)
Progressive disease	144 (37)
Not determined	39 (10)

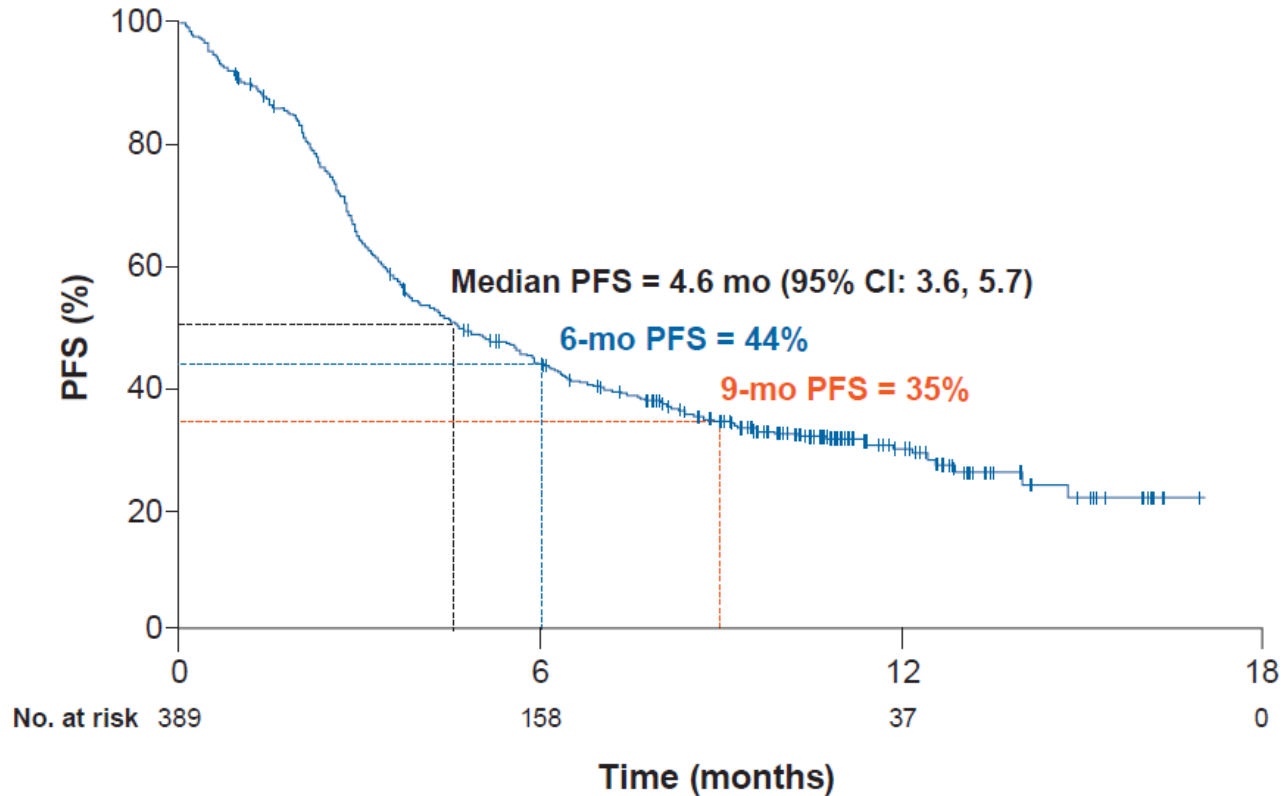
# Checkmate 025 Clinical Activity

Item	Nivolumab	Everolimus
<b>Objective response rate, %</b>	26	5
<b>Odds ratio (95% CI)</b>	6.13 (3.77–9.95)	
<b>P value</b>	<0.0001	
<b>Best overall response, %</b>		
Complete response	1	<1
Partial response	25	5
Stable disease	34	56
Progressive disease	35	27
Not evaluated	6	11
<b>Median duration of response, months (range)</b>	12.0 (0.0–36.8+)	12.0 (0.0+–33.0+)
<b>Ongoing response, n/N (%)</b>	30/105 (29)	3/22 (14)

# Kaplan–Meier estimate of OS



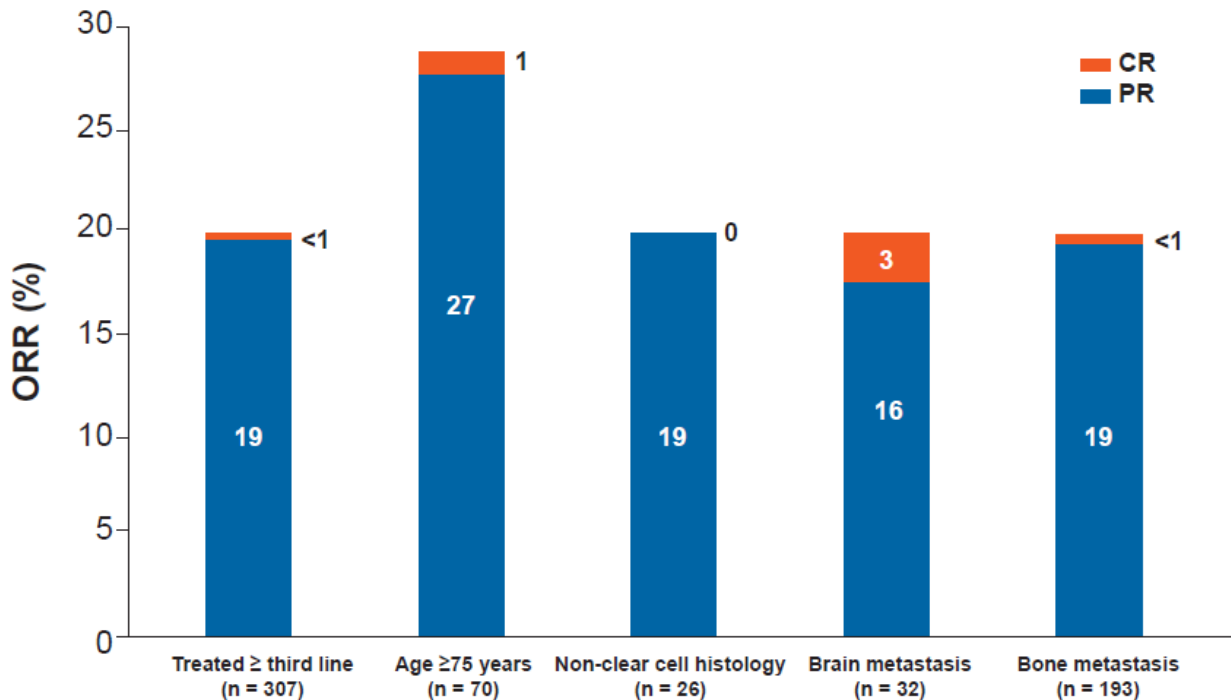
# Kaplan–Meier estimate of PFS



# Results: Impact of Baseline Characteristics on Efficacy

Response rates were comparable among patient subgroups based on previous lines of therapy, age, histology, and brain or bone metastasis

## ORR in select subpopulations



# Treatment-related AEs in $\geq 1\%$ of patients

Treatment-related AE	Any grade (N = 389)	Grade 3–4 (N = 389)
<b>Total, n (%)</b>	124 (32)	27 (7)
<b>General, n (%)</b>	60 (15)	9 (2)
Fatigue/asthenia	49 (13)	9 (2)
Pyrexia	12 (3)	0
Lack of appetite/anorexia	5 (1)	1 (<1)
<b>Skin and mucosal, n (%)</b>	38 (10)	2 (<1)
Rash	34 (9)	2 (<1)
<b>Gastrointestinal, n (%)</b>	33 (8)	5 (1)
Diarrhea	18 (5)	3 (1)
Nausea/vomiting	8 (2)	2 (<1)
<b>Pain, n (%)</b>	7 (2)	0
<b>Endocrine, n (%)</b>	12 (3)	1 (<1)
Hypothyroidism	6 (2)	0
Hyperthyroidism	6 (2)	0
Autoimmune hypophysitis	1 (<1)	1 (<1)
<b>Respiratory/pulmonary, n (%)</b>	7 (2)	3 (1)
Pneumonitis	3 (1)	1 (<1)
<b>Hematologic, n (%)</b>	11 (3)	3 (1)
Anemia	9 (2)	3 (1)
<b>Hepatic/pancreatic, n (%)</b>	9 (2)	0
Increased transaminase	5 (1)	0

# Conclusions

- ✓ To date these data represents **the most extensive reported real-world experience** with nivolumab in pre-treated RCC pts.
- ✓ These first data seem to confirm **efficacy** and **safety** data of the pivotal trial in a real world setting.
- ✓ Results in patient *populations poorly (**elderly or bone metastases**) or not represented at all (**brain metastases, non clear cell histology, pre-treated with everolimus**) in the pivotal trial* encourage the use of nivolumab in these subgroups of RCC pts.

# Grazie!

Ugo De Giorgi

Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori

IRST IRCCS – Meldola

[ugo.degiorgi@irst.emr.it](mailto:ugo.degiorgi@irst.emr.it)