DigiCore

IDEAL4RWE

***Immunotherapy in recurrent/metastatic head and neck cancer**: real-world data from ~~six~~ **nine** European countries (2017-2022)*

Presentation for Connect2Win, Madrid, 13 Nov 2023
Gaber Plavc, Rita Callisto, Elin Hallan Naderi

The IDEAL4RWE head and neck cancer team and collaborators

- Gaber Plavc (radiation oncologist)
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- Rita Silva Calisto (biostatistician/data scientist)
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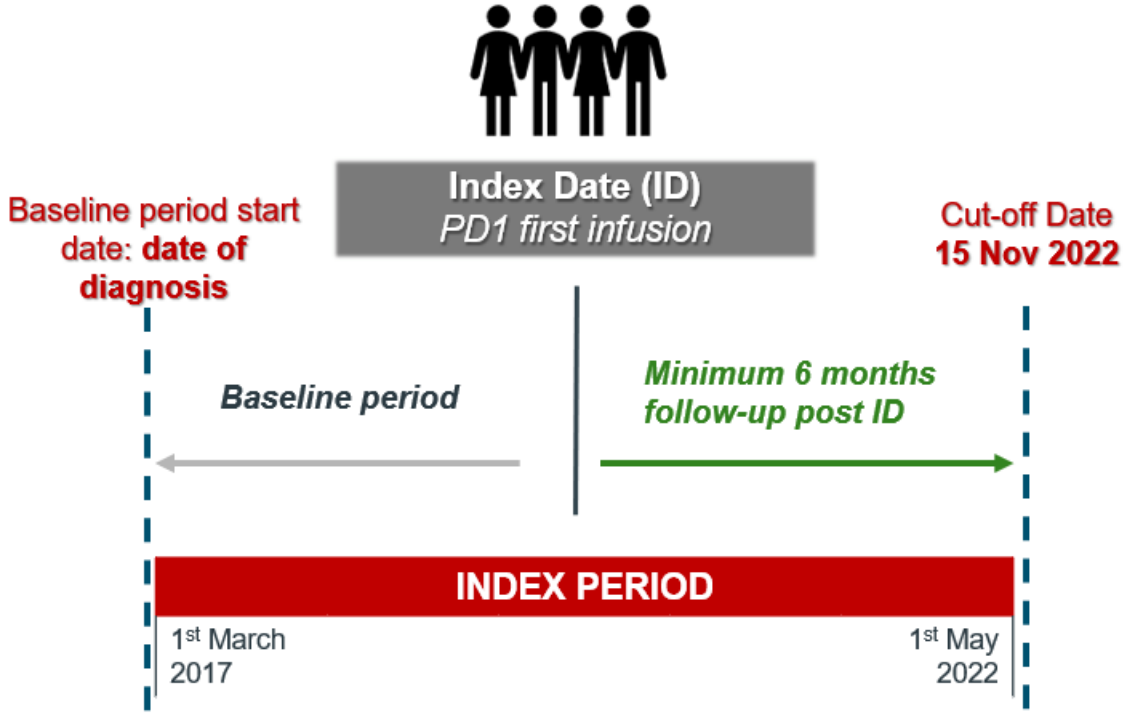
- Chiara Paratore (medical oncologist)
  - **San Luigi Gonzaga Hospital / Mauriziano Umberto I Hospital, University of Turin**
- Julia Lostes Bardaji (medical oncologist)
  - **Vall d´Hebron Institute of Oncology**
- Elin Hallan Naderi (clinical oncologist)
  - **Oslo University Hospital, Institute of Oncology**
- Collaborators:
  - Tomasz Rutkowski **(Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Poland)**
  - Kieran Zucker **(Leeds Teaching Hospitals NHS Trust, UK)**
  - Séverine Carlier and Cédric van Marcke de Lummen **(Cliniques universitaires Saint-Luc, Brussels, Belgium)**
  - Marie Bonnet and Andy Karabajakian **(Centre Léon Bérard, Lyon, France)**

Immunotherapy in patients with recurrent or metastatic HNSCC

- Are we treating the same patients?
- Are we using the same treatment approach?
- Are we using immunotherapy in the same way, and do we observe the same irAE?
- How do the treatment results of immunotherapy compare to what has been demonstrated in phase III clinical trials?



Methodology

~500 patients

Data collection at each collaborating Centre

General Patient Characteristics

Patient characteristics at Immunotherapy initiation

Treatments

Follow-up

Transfer of aggregated data to IPO

Only aggregated data/results will be transferred

Publication of the results

ESMO 2023

ICHNO

Scientific paper

Based on a R software script shared across sites

Time-dependent outcomes (rwPFS, TTNT, OS, TTD)

Descriptive analysis of cohort

Data Analysis at each collaborating Centre

Comparing between/within countries

Meta-analysis

Description of the findings and revision of data

ESMO 2023 poster (data from Slovenia, Italy, Portugal, Norway and Poland)

 # 933P

Real-World Patterns of Immunotherapy Utilization and Outcomes in Recurrent/Metastatic Head and Neck Cancer (R/M HNC) Patients across European Countries: A multicenter Retrospective Federated Analysis

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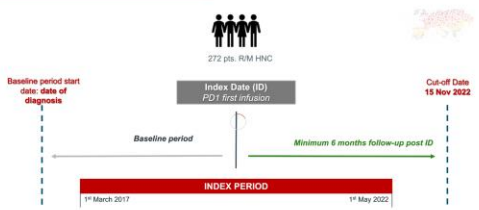
Keywords: Head and neck cancer, Immunotherapy, Real-World Data

BACKGROUND

» The number of real-world studies in oncology has widely increased in the last years, including in R/M HNC.
» Limited real-world data exists on treatment patterns and outcomes in R/M HNC pts receiving anti-PD-1 immunotherapy (IT).
» This study provides insights into contemporary IT use and sequencing. Preliminary results from five centers in five European countries (Italy, Poland, Portugal, Slovenia, Norway) are presented.

METHODS



» Retrospective data was collected from electronic health records (EHR) to a common data model (CMD) for R/M HNC pts who received IT between March 2017 and May 2022. (Fig 1).
» The data were analyzed at each site using a common R script and then each center transferred only the aggregated data to IPO-Porto to complete the analysis.
» Overall survival (OS) and real-world progression-free survival (rwPFS) were calculated from IT start.
» Lines of systemic therapy (line) included concomitant chemotherapy (ChT) used with radiotherapy (CRT).

RESULTS

» STUDY POPULATION

A total of 272 pts with a median age of 58.5–67.0 yrs were included (Table 1). 50.4% of pts had metastatic disease at IT start, 57.0% had platinum refractory disease, and 28.3% were tested for PD-L1 expression. 10.7% of pts began their treatment with IT, whereas most pts received anti-PD-1 after previous CRT or as a 2nd line (Pembrolizumab 7.7%, Pembrolizumab+ChT 3.3%, Nivolumab 31.9%). In the first line, the most common systemic treatments beside platinum CRT (40.1%) were platinum-containing combination ChT without cetuximab (31.0%) and ChT + cetuximab (10.6%). Overall, the maximum number of lines was 10 (Table 2) and Nivolumab was the most used agent (23.8%) followed by non-platinum mono chemotherapy (18.7%). Table 3 and Table 4 describe the types of IT and duration of IT in the different centers.

RESULTS

Table 1. Population description

	Oslo University Hospital Norway N=48	Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy N=23	Maria Sklodowska-Curie Institute - Oncology Center Poland N=69	Instituto Português de Oncologia do Porto Portugal N=54	Institute of Oncology Ljubljana Slovenia N=78
Sex					
Female	15 (20.8%)	6 (26.1%)	19 (27.5%)	9 (7.4%)	9 (11.5%)
Male	58 (79.2%)	17 (73.9%)	50 (72.5%)	50 (92.6%)	69 (88.5%)
Stage at diagnosis					
I	4 (5.6%)	1 (4.3%)	2 (2.9%)	2 (3.7%)	0 (0.0%)
II	6 (12.7%)	3 (13.0%)	0 (0%)	2 (3.7%)	10 (12.8%)
III	16 (33.3%)	7 (30.4%)	3 (4.3%)	4 (7.4%)	9 (11.5%)
IV	39 (81.7%)	12 (52.2%)	64 (92.8%)	46 (88.9%)	59 (75.6%)
HPV Status at diagnosis					
Positive	12 (25.0%)	4 (17.4%)	4 (5.8%)	2 (3.7%)	12 (15.4%)
Negative	3 (6.3%)	6 (26.1%)	14 (20.3%)	16 (29.6%)	21 (32.1%)
Unknown	33 (68.8%)	13 (56.5%)	51 (73.9%)	36 (66.7%)	45 (57.6%)
Smoking status at diagnosis					
Yes, currently	22 (45.8%)	10 (43.5%)	21 (30.4%)	29 (53.7%)	39 (50.0%)
Yes, previously	13 (27.1%)	9 (26.1%)	32 (46.4%)	19 (35.2%)	26 (33.3%)
Never	13 (27.1%)	3 (13.0%)	16 (23.2%)	6 (11.1%)	4 (7.7%)
Unknown	0 (0%)	4 (17.4%)	1 (1.4%)	0 (0%)	9 (0.4%)
Age at index					
Median (Min, Max)	65.0 (45.0, 82.0)	67.0 (39.0, 79.0)	61.0 (29.0, 80.0)	58.5 (36.0, 79.0)	59.5 (28.0, 76.0)
ECOG at index					
0	13 (27.1%)	6 (26.1%)	19 (30.8%)	9 (9.3%)	6 (7.7%)
1	25 (52.1%)	14 (60.9%)	56 (81.2%)	42 (77.8%)	53 (75.6%)
2	9 (18.8%)	2 (8.7%)	0 (0%)	7 (13.0%)	11 (14.7%)
3	1 (2.1%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)
Disease location at index					
Locoregional disease and distant metastases	14 (29.2%)	8 (34.8%)	16 (24.2%)	16 (27.8%)	20 (26.6%)
Locoregional only	8 (12.5%)	5 (21.7%)	15 (21.7%)	6 (11.1%)	13 (16.7%)
Regional lymph nodes only	0 (0%)	2 (8.7%)	5 (7.2%)	4 (7.4%)	8 (10.3%)
Distant metastases only	9 (18.8%)	2 (8.7%)	7 (10.1%)	9 (16.7%)	17 (21.8%)
Local tumor and distant metastases	8 (12.5%)	6 (17.4%)	3 (4.3%)	4 (7.4%)	1 (1.3%)
Local tumor only	5 (10.4%)	2 (8.7%)	14 (22.2%)	5 (9.3%)	14 (17.9%)
Regional lymph nodes and distant metastases	9 (18.7%)	0 (0%)	7 (10.1%)	11 (20.4%)	5 (6.4%)
Treatment response at index					
Platinum-refractory	10 (20.8%)	13 (56.5%)	54 (80.3%)	37 (68.5%)	37 (47.4%)
Sensitive	38 (79.2%)	10 (43.5%)	11 (15.9%)	16 (29.6%)	41 (52.6%)

Table 2 Number of Lines of treatment per different

	Line of Treatment (SACT)									
	Lot 1	Lot 2	Lot 3	Lot 4	Lot 5	Lot 6	Lot 7	Lot 8	Lot 9	Lot 10
Oslo University Hospital Norway	48 (100%)	40 (83.3%)	0 (18.8%)	7 (14.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy	23 (100%)	18 (78.3%)	7 (30.4%)	5 (21.7%)	2 (8.7%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Maria Sklodowska-Curie Institute - Oncology Center Poland	69 (100%)	69(100%)	41 (59.4%)	20 (29.0%)	7 (10.1%)	2 (2.9%)	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)
Instituto Português de Oncologia do Porto Portugal	54 (100%)	54(100%)	38 (70.4%)	26 (48.1%)	21 (38.9%)	10 (18.5%)	4 (7.4%)	2 (3.7%)	2 (3.7%)	1 (1.9%)
Institute of Oncology Ljubljana Slovenia	78 (100%)	69 (88.5%)	53 (67.9%)	34 (43.6%)	19 (24.4%)	10 (12.%)	3 (3.8%)	1 (1.3%)	0 (0%)	0 (0%)

» TIME TO EVENT RESULTS

Median overall survival from anti-PD-1 initiation across countries was 5.9–13.6 months (ms), and the median rwPFS ranged 2.8–4.8 ms. ***(Table 5)***

» REAL WORLD IMMUNE-RELATED ADVERSE EFFECTS (IRAES) REPORTED

The overall occurrence of irAEs ranged 18.3–81.3% across countries, with the most common irAEs being endocrinal disorders (42.0%), gastrointestinal (26.8%), blood and lymphatic (26.8%) disorders, and investigations. The irAEs were most commonly grade 1 (57.7%), followed by grade 2 (32.9%), grade 3 (7.1%), and grade 4 (0.4%). No irAEs grade 5 were reported. ***(Fig 2)***

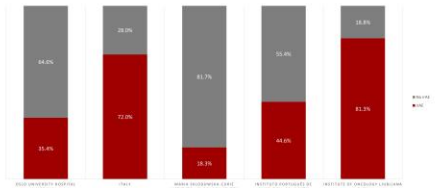


Fig 2. Occurrence of irAE effect by centre

Table 3. Distribution of type of IT regimen per centre

	Oslo University Hospital Norway	Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy	Maria Sklodowska-Curie Institute - Oncology Center Poland	Instituto Português de Oncologia do Porto Portugal	Institute of Oncology Ljubljana Slovenia
SACT prior IT (Curative)					
Num of patients	25 (52.1%)	8 (34.8%)	53 (76.8%)	29 (53.7%)	49 (62.8%)
Type of IT regimen used					
Pembrolizumab monotherapy	23 (47.9%)	8 (32.0%)	1 (1.4%)	29 (35.4%)	11 (13.8%)
Platinum/5FU/pembrolizumab	10 (20.8%)	3 (12.0%)	1 (1.4%)	0 (0%)	14 (17.5%)
Nivolumab monotherapy	15 (31.3%)	14 (56.0%)	69 (97.2%)	53 (64.6%)	55 (68.8%)

Table 4. Duration of treatment of different types of IT per centre

	Oslo University Hospital Norway	Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy	Maria Sklodowska-Curie Institute - Oncology Center Poland	Instituto Português de Oncologia do Porto Portugal	Institute of Oncology Ljubljana Slovenia
Duration of treatment (days)					
Nivolumab monotherapy	**(N=15)**	**(N=14)**	**(N=69)**	**(N=53)**	**(N=55)**
Median [Min, Max]	56.0 [0, 707]	86.0 [0, 790]	Not Avalible	60.0 [0, 1330]	90.0 [0, 769]
Pembrolizumab monotherapy	**(N=23)**	**(N=8)**	**(N=1)**	**(N=3)**	**(N=11)**
Median [Min, Max]	168 [0, 546]	103 [21.0, 281]	Not Availabel	21.0 [0, 29.0]	105 [20.0, 420]
Platinum/5FU/pembrolizumab	**(N=10)**	**(N=3)**	**(N=1)**	**(N=0)**	**(N=14)**
Median [Min, Max]	89.5 [0, 325]	112 [74.0, 592]	Not available	-	137 [46.0, 677]

Table 5. Overall survival and Progression Free Survival per country

	Oslo University Hospital Norway N=48	Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy N=23	Maria Sklodowska-Curie Institute - Oncology Center Poland N=69	Instituto Português de Oncologia do Porto Portugal N=54	Institute of Oncology Ljubljana Slovenia N=78
Overall Survival					
Median Survival (months)	10.2	14.5	5.9	7.9	11.6
Overall Survival (%) at 1 year	45.1%	55.8%	32.9%	28.8%	48.8%
Patients at risk					
1 year	20	10	21	13	27
2 year	1	4	10	6	4
rwProgression Free Survival					
Median rwPFS (months)	5.2	5.1	3.7	2.8	4.8
rwPFS (%) at 1 year	20.3%	36.0%	22.6%	9.4%	23.1%
Patients at risk					
1 year	7	6	8	3	10
2 year	7	2	4	3	2

CONCLUSIONS

»This real-world study across five European countries shows variable IT utilization and outcomes, irAEs occurrence, and treatment patterns in R/M HNC patients

»Real-world outcomes of this Study in R/M HNC are similar to outcomes in randomized control trials in R/M HNC

»Further research is needed to optimize IT use, considering patient characteristics and treatment factors

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Sex					
Female	10 (20.8%)	6 (26.1%)	19 (27.5%)	4 (7.4%)	9 (11.5%)
Male	38 (79.2%)	17 (73.9%)	50 (72.5%)	50 (92.6%)	69 (88.5%)
Stage at diagnosis					
I	6 (12.5%)	1 (4.3%)	2 (2.9%)	2 (3.7%)	3 (3.8%)
II	6 (12.5%)	3 (13.0%)	0 (0%)	0 (0%)	10 (12.8%)
III	16 (33.3%)	7 (30.4%)	3 (4.3%)	4 (7.4%)	9 (11.5%)
IV	20 (41.7%)	12 (52.2%)	64 (92.8%)	48 (88.9%)	56 (71.8%)
HPV Status at diagnosis					
Positive	12 (25.0%)	4 (17.4%)	4 (5.8%)	2 (3.7%)	12 (15.4%)
Negative	3 (6.3%)	6 (26.1%)	14 (20.3%)	16 (29.6%)	25 (32.1%)
Unknown	33 (68.8%)	13 (56.5%)	51 (73.9%)	36 (66.7%)	41 (52.6%)
Smoking status at diagnosis					
Yes, currently	22 (45.8%)	10 (43.5%)	21 (30.4%)	29 (53.7%)	39 (50.0%)
Yes, previously	13 (27.1%)	6 (26.1%)	22 (31.9%)	19 (35.2%)	28 (35.9%)
Never	13 (27.1%)	3 (13.0%)	25 (36.2%)	6 (11.1%)	6 (7.7%)
Unknown	0 (0%)	4 (17.4%)	1 (1.4%)	0 (0%)	5 (6.4%)
Age at index					
Median [Min, Max]	65.0 [45.0, 82.0]	67.0 [39.0, 79.0]	61.0 [29.0, 80.0]	58.5 [26.0, 79.0]	59.5 [28.0, 76.0]
ECOG at index					
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2	9 (18.8%)	2 (8.7%)	0 (0%)	7 (13.0%)	13 (16.7%)
3	1 (2.1%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)
Disease location at index					
Locoregional disease and distant metastases	14 (29.2%)	8 (34.8%)	16 (23.2%)	15 (27.8%)	20 (25.6%)
Locoregional only	6 (12.5%)	5 (21.7%)	15 (21.7%)	6 (11.1%)	13 (16.7%)
Regional lymph nodes only	0 (0%)	2 (8.7%)	5 (7.2%)	4 (7.4%)	8 (10.3%)
Distant metastases only	9 (18.8%)	2 (8.7%)	7 (10.1%)	9 (16.7%)	17 (21.8%)
Local tumor and distant metastases	6 (12.5%)	4 (17.4%)	3 (4.3%)	4 (7.4%)	1 (1.3%)
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Regional lymph nodes and distant metastases	8 (16.7%)	0 (0%)	7 (10.1%)	11 (20.4%)	5 (6.4%)
Platinum sensitivity at index					
Platinum-refractory	10 (20.8%)	13 (56.5%)	58 (84.1%)	37 (68.5%)	37 (47.4%)
Sensitive	38 (79.2%)	10 (43.5%)	11 (15.9%)	16 (29.6%)	41 (52.6%)

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Maria Sklodowska-Curie Institute - Oncology Center Poland	69 (100%)	69(100%)	41 (59.4%)	20 (29.0%)	7 (10.1%)	2 (2.9%)	1 (1.4%)	0 (0%)	0 (0%)	0 (0%)
Instituto Português de Oncologia do Porto Portugal	54 (100%)	54(100%)	38 (70.4%)	26 (48.1%)	21 (38.9%)	10 (18.5%)	4 (7.4%)	2 (3.7%)	2 (3.7%)	1 (1.9%)
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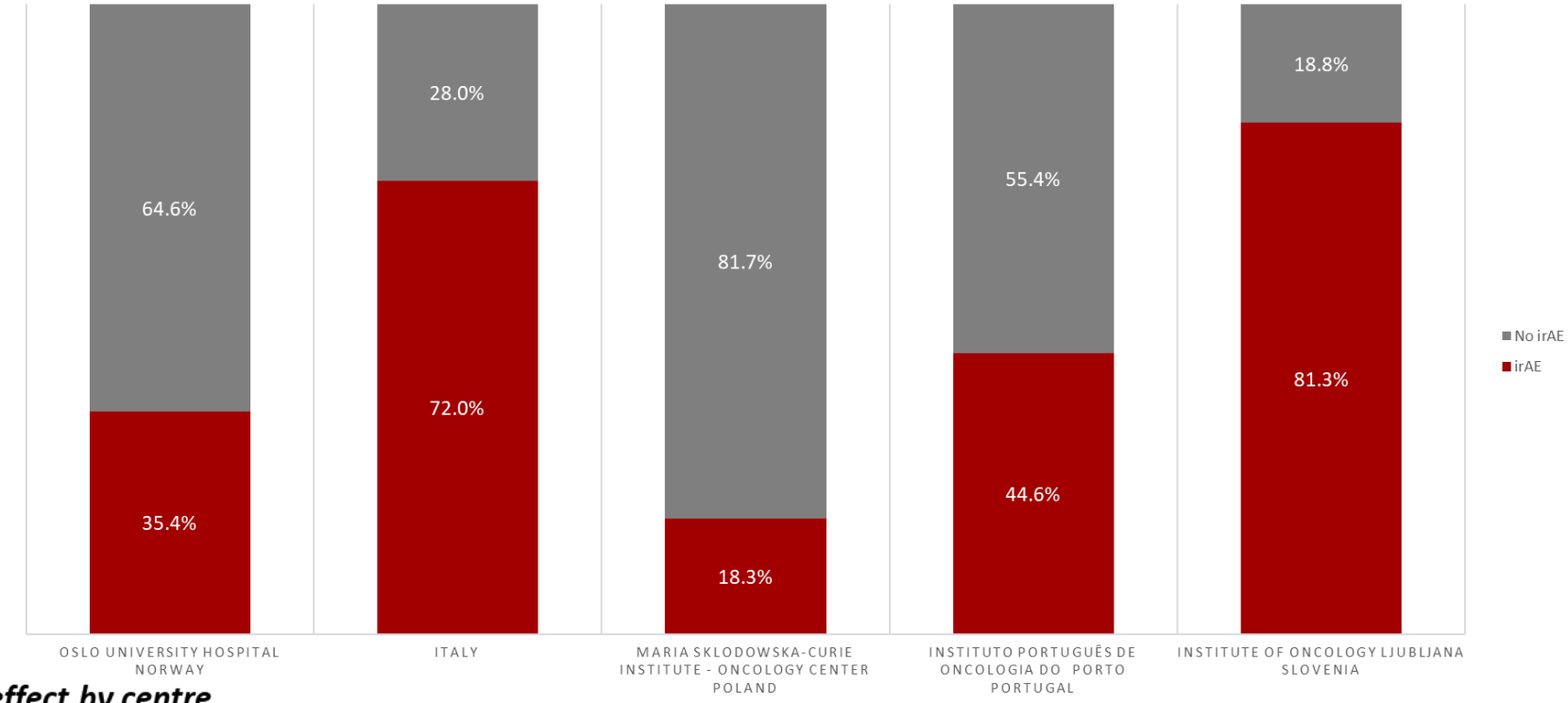

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	Oslo University Hospital Norway N=48	Azienda Ospedaliera Ordine Mauriziano +Azienda Ospedaliera Universitaria San Luigi Gonzaga Italy N=23	Maria Sklodowska-Curie Institute - Oncology Center Poland N=69	Instituto Português de Oncologia do Porto Portugal N=54	Institute of Oncology Ljubljana Slovenia N=78
Overall Survival					
Median Survival (months)	10.2	14.5	5.9	7.9	11.6
Overall Survival (%) at 1 year	45.1%	55.8%	32.9%	28.8%	48.8%
Patients at risk					
1 year	20	10	21	13	27
2 year	1	4	10	6	4
rwProgression Free Survival					
Median rwPFS (months)	5.2	5.1	3.7	2.8	4.8
rwPFS (%) at 1 year	20.3%	36.0%	22.6%	9.4%	23.1%
Patients at risk					
1 year	7	6	8	3	10
2 year	7	2	4	3	2

Publication of Results

ESMO 2023	Scientific Paper
• Abstract successfully presented as poster	• Aim to submit manuscript by Q4 2023

Opportunities & Challenges (as presented in Frankfurt March 2023)

Networking

- Exchanging clinical and research experience with peers and discussing open questions within a diverse team
- Good basis for future research collaboration
  - › Projects on rare HN cancers

In active talks with IDEAL4RC and EURACAN

The research group originally included centres from 5 different countries, at the moment 9 & can be easily expanded by inclusion of additional research centres in the future

Challenges

- Expertise in RWE research (learning as we go along...)
- **Structured data (a lot of manual extraction needed across the centres)**
- **Data quality could be better**
- Comparability across sites (differences in drugs reimbursements, differences in requirements of ethical committees...)
- Distance & Time (even dedicated time for research at workplace can be interrupted by clinical call)