RAMUCIRUMAB/PACLITAXEL THERAPY IN PATIENTS WITH ADVANCED GASTRIC CARCINOMA OR GASTROESOPHAGEAL JUNCTION (GEJ) ADENOCARCINOMA IN THE CZECH REPUBLIC – PATIENT CHARACTERISTICS AND TREATMENT OUTCOMES

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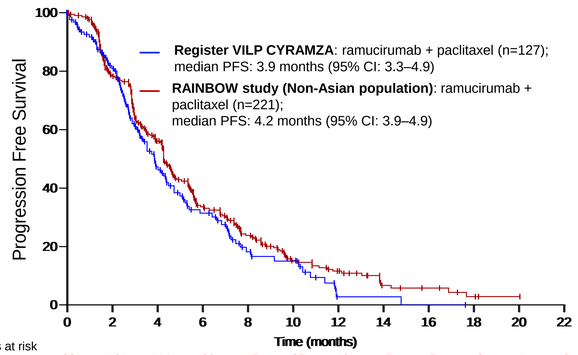
INTRODUCTION

- In the Czech Republic, real-world clinical practice data collection is a condition required for temporary drug reimbursement
- The Health Insurance Bureau in collaboration with The Institute of Biostatistics and Analyses from Masaryk University, Brno, initiated the 'CYRAMZA VILP' patient registry focusing on ramucirumab in combination with paclitaxel for the treatment of advanced gastric carcinoma or GEJ adenocarcinoma. Together, they conducted an independent assessment of the real-world outcomes of this treatment in patients meeting reimbursement criteria and treated under VILP reimbursement regimen, with the intention of informally examining whether the progression free survival (PFS) in the registry is in agreement with the PFS in the non-Asian subgroup of the phase 3 registrational trial, RAINBOW (NCT01170663)[1]
- Here we report the registry outcomes based on data collected between February 1, 2018 and March 2, 2020 in light of the results from the non-Asian patient subgroup in the RAINBOW trial

KEY RESULTS

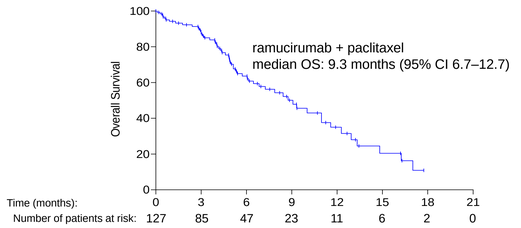
PFS of patients treated within the VILP in the Czech Republic (n=127) and the non-Asian population from the registrational trial, RAINBOW (n=221)*



Time (months) :	0	2	4	6	8	10	12	14	16	18	20	22
Number of patients at risk												
RAINBOW (Non-Asian population) :	221	164	114	66	47	27	18	7	5	3	1	0
Register VILP CYRAMZA :	127	89	44	27	13	10	1	1	1	0	-	-

At time of analysis, disease progression or death were recorded in 89 (70.1%) of the total of 127 patients in the registry
***Registry and clinical trial populations were not adjusted for patient characteristics**

Overall survival (OS) of patients from the Czech register VILP CYRAMZA (n=127)



Time (months):	0	3	6	9	12	15	18	21
Number of patients at risk:	127	85	47	23	11	6	2	0

At time of analysis, there were 53 deaths (41.7%) from the total of 127 patients in the registry
Median OS in non-Asian RAINBOW subgroup was 8.5 months (95% CI 7.4 - 9.8)*
***Registry and clinical trial populations were not adjusted for patient characteristics**

Best Achieved Response to treatment*	**N = 78** n (%)
Complete response (CR)	0 (0.0)
Partial response (PR)	16 (20.5)
Disease stabilization (DS)	35 (44.9)
Disease progression (DP)	27 (34.6)

* In patients with reported therapeutic response data

CONCLUSIONS

- Real-world data indicate that reimbursed treatment of advanced gastric or GEJ adenocarcinoma with ramucirumab and paclitaxel in the Czech Republic is effective
- Despite the limitations of this description (no formal comparisons or adjustments were made for differences between patient characteristics), reported outcomes from the ramucirumab and paclitaxel treatment registry appear to be generally consistent with the efficacy results for non-Asian patients in the registrational trial, RAINBOW and with previous published studies in real-life conditions from Europe[1,2,3]
- The low frequency of reported adverse events (3 evaluable reports out of 5 reported in total) may be due to non-obligatory reporting of safety data in this retrospective non-interventional patient registry

OBJECTIVES & METHODOLOGY

Registry Design

- Retrospective, non-interventional collection of data from treated patients

Reimbursement Criteria

- Ramucirumab plus paclitaxel combination treatment is reimbursed in adult patients with advanced stomach carcinoma or adenocarcinoma of GEJ, with disease progression after previous chemotherapy with the combination of platinum and fluoropyrimidine, and performance status Eastern Cooperative Oncology Group (ECOG) scale 0-1
- If it is necessary to suspend or discontinue the treatment with paclitaxel within the combined regimen due to paclitaxel toxicity, treatment with ramucirumab may continue if ramucirumab alone is well tolerated

Objectives

- Primary endpoint:
  - PFS (time from treatment initiation until the disease progression or death)
- Secondary endpoints:
  - OS (time from treatment initiation till death from any reason);
  - Response to Treatment;
  - Safety of treatment (frequency and severity of adverse events)

- The PFS reported for the subgroup of n=221 patients from Europe, Israel, Australia, United States of America, Argentina, Brazil, Chile, and Mexico in the registrational trial, RAINBOW (Wilke et al., 2014[1], NCT01170663) was used as a benchmark.

Methods

- The data have been summarized by means of standard descriptive statistics and frequency tables; absolute and relative number in case of categorial variables, average (95% confidence interval, CI) and median with range (minimum–maximum) in case of continuous variables

- The description of OS, PFS and Time on Treatment has been done by means of Kaplan-Meier (KM) survival curves and corresponding medians and 95%CI

Baseline Demographics and Disease Characteristics: Register VILP CYRAMZA

	N = 127 (100%) n (%) unless specified otherwise
Sex	
Male	83 (65.4)
Female	44 (34.6)
Age when starting treatment with ramucirumab, years	
≤ 50	23 (18.1)
51–60	29 (22.8)
61–70	47 (37.0)
> 70	28 (22.0)
Average (95% CI)	62.0 (60.2–63.8)
Median (min–max)	65 (38–78)
Time of monitoring since the initiation of therapy (months)	
Average (95% CI)	5.5 (4.7–6.3)
Median (min–max)	4.4 (0.0–18.7)
Time from diagnosis till ramucirumab therapy initiation (months)	
Average (95% CI)	16.1(12.6–19.7)
Median (min–max)	10.9 (2.4–185.0)
Performance Status (ECOG)	
0	52 (40.9)
1	75 (59.1)
Line of ramucirumab therapy (N = 126*)	
2nd line	116 (92.1)
3rd line and further	10 (7.9)
Year of starting ramucirumab treatment	
2017	5 (3.9)
2018	55 (43.3)
2019	59 (46.5)
2020	8 (6.3)
Treatment with ramucirumab in combination with paclitaxel	
no	1 (0.8)
yes	126 (99.2)
Metastases at the time of starting treatment with ramucirumab	
no	3 (2.4)
yes	124 (97.6)
Number of metastases (N = 122*)	
< 3 metastatic lesions	37 (30.3)
≥ 3 metastatic lesions	85 (69.7)
Peritoneal metastases (N = 122*)	
no	61 (50.0)
yes	61 (50.0)
Ascites (N = 126*)	
no	102 (81.0)
yes	24 (19.0)
Weight, kg (N = 126*)	
Average (95% CI)	73.5 (70.7–76.2)
Median (min–max)	70.5 (44.0–110.0)
Height, cm (N = 126*)	
Average (95% CI)	173.0 (171.3–174.7)
Median (min–max)	173.5 (150.0–197.0)

*patients with reported data

Baseline demographics and Disease Characteristics: RAINBOW (Non-Asian, ramucirumab-treated population)[4]

	N =221 n (%) unless specified otherwise
Sex	
Male	156 (71)
Female	65 (29)
Age, years	
Median (min–max)	60 (25-83)
Performance Status (ECOG)	
0	73 (33)
1	148 (67)
Year of starting ramucirumab treatment[1]	
2010	NR
2011	NR
2012	NR
Number of metastatic sites	
0-2	127 (57)
≥ 3	94 (43)
Presence of peritoneal metastases	
Yes	98 (44)
Presence of ascites	
Yes	75 (34)

Abbreviations: Adverse events, AE; Confidence interval, CI; Eastern Cooperative Oncology Group, ECOG; gastroesophageal junction, GEJ; Kaplan Meier, KM; Not reported, NR; Overall survival, OS; Progression free survival, PFS; State Institute for Drug Control, SÚKL; highly innovative drug product, VILP;

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Course of Treatment with ramucirumab: Register VILP CYRAMZA

	N = 127 (100%) n (%) unless specified otherwise
Ramucirumab-containing regimen	
8 mg/kg by IV on the 1st and 15th day of the 28-day cycle	127 (100)
Change of dosage	
No	126 (99.2)
Yes[a]	1 (0.8)
Treatment suspension	
No	120 (94.5)
Yes[b]	7 (5.5)
Time to treatment failure[c] (months)	
KM survival estimate : median (95% CI)	3.4 (2.7-4.1)
Treatment discontinued	
No	35 (27.6)
yes	92 (72.4)
Reason for discontinuation (n=92)	
Disease progression	69 (75)
Status deterioration without progression	15 (16.3)
Death	3 (3.3)
Other reasons[d]	5 (5.4)
Length of treatment (months) (n=92)	
Average (95% CI)	3.9 (3.2-4.6)
Median (min–max)	2.9 (0.0-17.7)

[a] The dose for the patient was changed due to thrombocytopenia
[b] Reasons included a request for reimbursement, neutropenia and stomatological intervention
[c] Time to treatment failure describes the time interval from treatment initiation until its discontinuation for any reason; described using
KM estimate of the probability of survival without an event
[d] Examples include disease stabilization, hepatorenal failure and urosepsis

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