#427P: Real World Data of trifluridine/tipiracil in refractory mCRC: a multicenter experience at four GEODA Spanish hospitals.

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INTRODUCTION

- TAS-102 (trifluridine/tipiracil) is approved as monotherapy in the treatment for patients with with metastatic colorectal cancer (mCRC) who have been previously treated or are not considered candidates for others treatment.
- Although it has been shown to improve overall survival (OS) and progression-free survival (PFS), it is not clear which patients may benefit from this drug in real-life clinical practice.

AIM

- To evaluate the safety and tolerability of TAS 102 in real-life clinical practice.
- Determine the which patient profile can benefit the most from the administration of TAS 102.
- Show our efficacy data with TAS 102 in mCRC.

METHOD

- We performed a multicenter, retrospective and observational analysis of 222 patients with mCRC receiving TAS-102 in various Spanish centers from November 2015 to the present.
- Previously, we prespecified a subgroup of patients “with low-volume metastatic disease”, defined as no massive hepatic metastasis or simultaneous liver and lung involvement
- Efficacy, toxicity, survival and patient profile data are evaluated.

RESULTS

222 patients with mCRC were avaluated. Baseline demographic and disease characteristics of our population are represented in table 1.

TAS-102 was very well tolerated (Table 2). A dose reduction was required in 34.7% of patients but only 4.1% discontinued therapy due to toxicity. Toxicity included fatigue 57.8% (G3 5.1%), nausea 24.7% (G3 0.9%) and diarrhea 21.5% (G3 0.5%). Neutropenia was common 74.1% (≥ G3 20.2%).

After a median of 3 cycles (2-23), median duration of treatment was 4.4 months (m) (1.2-26.2), with a disease control rate (DCR) of 33.8%. Partial response (ORR) achieved in 1.8%. Median PFS of 3.9m (95% CI 3.5-4.2) and median OS of 9.3m (95% CI 7.9-10.67) were observed in our analysis (Table 3). There was no statistically significant difference of PFS and OS according to primary tumor location or RAS/BRAF mutation status, although Mismatch Repair Proficient (MMRp) tumors was associated with longer PFS (6.1 vs 3.4m, respectively, p=0.002) and OS (14.2 vs 6.3, p=0.001).

Patients with low-volume metastatic disease had better DCR than patients with high volume (44,9% vs 24,2%, respectively, p=0.03) and PFS and OS were also significantly better for patients with low-volume metastatic disease with PFS 4.1 vs 3.5m, respectively (p=0.024, HR 1.73 95%CI 1.04-1.81) and OS 11.7 vs 7.8m, respectively (p=0.012 HR 1.49 95%CI 1.08-2.3) (Table 5).

In the subgroup of who received prolonged treatment (6 cycle or more, N=51), 43.1% were <65 years, 60.8% had low-volume metastatic disease and 54.9% of patients had received TAS102 as second and third line. Almost all patients in this subgroup (92.2%) presented stable disease and PFS was significantly higher than in subgroup of patients who received 5 or fewer cycles (9.3 vs 3.36 m, p<0.001, HR 0.15 95%CI 0.1-0.2) and higher OS (15.9 vs 7.46m, p< 0.001, HR 0.35 95%ci 0.24-0.52). (Table 4).

Baseline Characteristics of the Population	
Age (yr) – median	62 (31-83)
Sex (%)	
Male	62.6%
Female	37.4%
Primary site of disease (%)	
Right	25.2%
Left	74.8%
RAS Mutation	57.2%
BRAF Mutation	2.3%
MMRp	9.0%
Number of prior regimens – no. (%)	
3	121 (54.5)
≥4	65 (29.3)

Table 1. Demographic and disease characteristics of our population.

Population with better outcomes
• Low-volume metastatic disease
• Received TAS102 as second and third line

Table 4. Characteristics of the population with the best prognosis after statistical analysis

Toxicity	Our population	Recourse
Fatigue	57.8%	35%
Grade ≥ 3	5.1%	4%
Diarrhea	21.5%	32%
Grade ≥ 3	0.5%	3%
Nausea	24.7%	48%
Grade ≥ 3	0.9%	2%
Neutropenia	74.1%	67%
Grade ≥ 3	20.2%	38%
Dose reduction	34.7%	14%
Discontinuation	4.1%	4%

Table 2. Comparison between the safety and toxicity found in our population and the Recourse trial.

	Our population	Recourse
ORR	1.8%	1.6%
DCR	33.8%	44%
PFS	3.9m (95% CI 3.5-4.2)	2m (95% CI 1.9-2.1)
OS	9.3m (95% CI 7.9-10.67)	7.1m (95% CI 6.5-7.8)

Table 3. Comparison between the efficacy found in our population and the Recourse trial.

Efficacy in the subgroup with better outcomes (N=98)	
DCR	44.9%
PFS	4.1m
OS	11.7m

Table 5. Efficacy of TAS 102 in the subgroup with the best prognosis

CONCLUSIONS

- The OS and PFS observed in our real-world experience were consistent with the RECOURSE trial, although in our RWD were slightly higher.
- TAS-102 showed a reasonable safety profile and the most prevalent adverse events seen in our patients were in keeping with those reported in the approval clinical trial.
- The subgroup that obtained the greatest benefit with TAS-102 was: < 65 years, low-volume metastatic disease and received as second and third line.

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