Safety and efficacy of telaprevir or boceprevir in combination with peginterferon alfa/ribavirin, in 497 cirrhotic non responders. Week 16 analysis of the French early access program (ANRS CO20-CUPIC) in real-life setting)

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Abstract 51

French Early Access Program

ATU

The Temporary Authorization for Use (ATU) is an early access program for medicinal products which have undergone full clinical development and are waiting for marketing authorization by the French Health Products Safety Agency (ANSM)

CUPIC

Compassionate Use of Protease Inhibitors in viral C Cirrhosis

National multicenter observatory in the setting of the ATU

Promoter: ANRS

Aim: to prospectively collect clinical data and biological specimen

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CUPIC Patients

- Treated in the French early access program
- HCV genotype 1 patients
- Compensated cirrhosis (Child Pugh A)
- Non-responders
  - Relapsers
  - Partial responders
    (↓ >2 log10 HCV RNA decline at Week 12)
  - Null responders initially excluded

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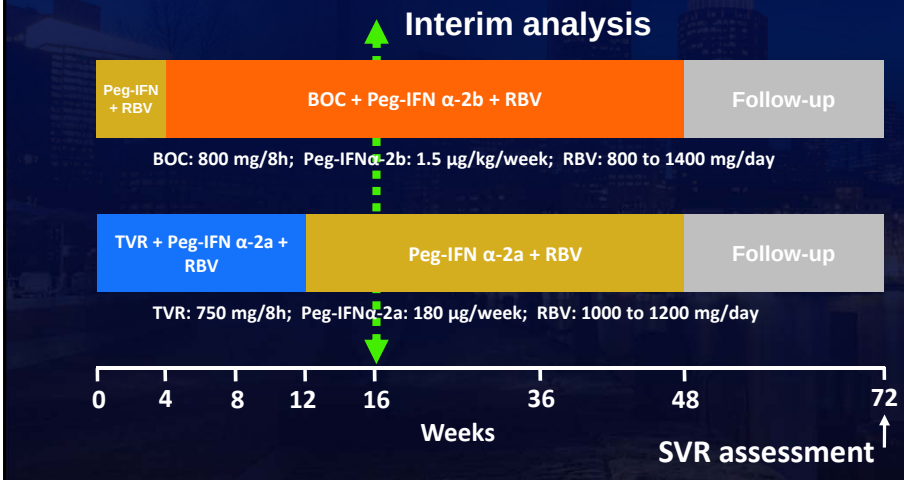
Treatment regimen



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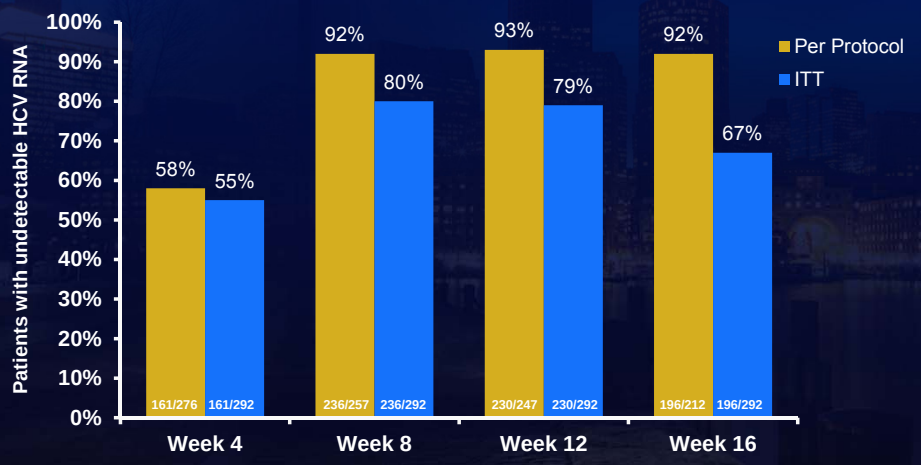
Telaprevir: week 16 efficacy data



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Telaprevir: week 16 safety findings

Patients, n (% patients with at least one event)	Telaprevir n=292
Serious adverse events (SAEs)*	132 (45.2%)
Premature discontinuation Due to SAEs	66 (22.6%) 43 (14.7%)
Death Septicemia, Septic shock, Pneumopathy, Endocarditis, Oesophageal varices Bleeding,	5 (2.6%)
Infection (Grade 3/4)	19 (6.5%)
Hepatic decompensation (Grade 3/4)	6 (2.0%)
Asthenia (Grade 3/4)	16 (5.5%)
Rash Grade 3/SCAR	14 (4.8%)
Renal failure	5 (1.7%)

*334 SAEs in 132 patients; SCAR: severe cutaneous adverse reaction

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Telaprevir: week 16 safety findings

Patients, n (% patients with at least one event)	Telaprevir n=292
Anemia	
Grade 2 (8.0 – ≤9.0 g/dL)	55 (18.8%)
Grade 3/4 (<8,0 g/dL)	34 (11.6%)
EPO use	157 (53.8%)
Blood transfusion	47 (16.1%)
RBV dose reduction	38 (13.0%)
Neutropenia	
Grade 3 (500 – <750/mm^3)	6 (2.0%)
Grade 4 (<500/mm^3)	2 (0.7%)
G-CSF use	7 (2.4%)
Thrombocytopenia	
Grade 3 (20,000 – <50,000/mm^3)	28 (9.6%)
Grade 4 (<20,000/mm^3)	9 (3.1%)
Thrombopoïetin Use	4 (1.4%)

EPO: Erythropoïetin; G-CSF: granulocyte-colony stimulating factor

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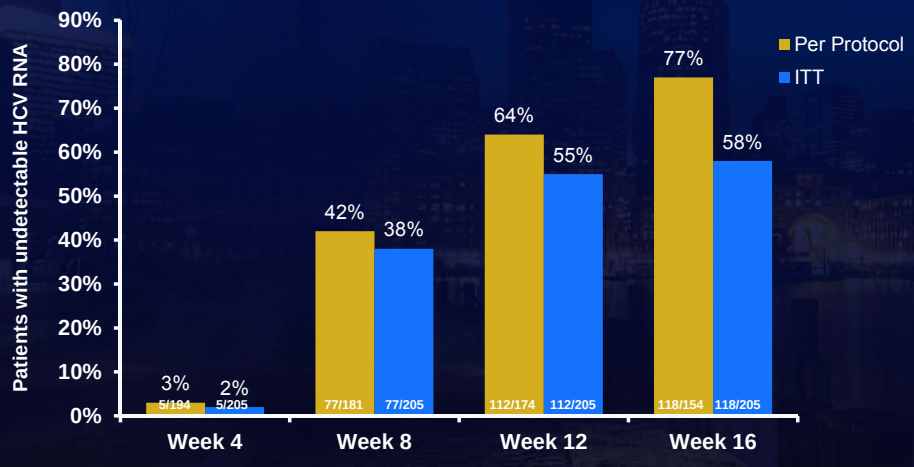
Boceprevir: week 16 efficacy data



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Boceprevir: week 16 safety findings

Patients, n (% patients with at least one event)	Boceprevir n=205
Serious adverse events (SAEs)*	67 (32.7%)
Premature discontinuation Due to SAEs	54 (26.3%) 15 (7.3%)
Death Pneumopathy	1 (0.5%)
Infection (Grade 3/4)	5 (2.4%)
Hepatic decompensation (Grade 3/4)	6 (2.9%)
Asthenia (Grade 3/4)	12 (5.8%)
Rash Grade 3/SCAR	 0
Renal failure	0

*159 SAEs in 67 patients; SCAR: severe cutaneous adverse reaction

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Boceprevir: week 16 safety findings

Patients, n (% patients with at least one event)	Boceprevir n=205
Anemia	
Grade 2 (8.0 – ≤9.0 g/dL)	48 (23.4%)
Grade 3/4 (<8,0 g/dL)	9 (4.4%)
EPO use	95 (46.3%)
Blood transfusion	13 (6.3%)
RBV dose reduction	22 (10.7%)
Neutropenia	
Grade 3 (500 – <750/mm^3)	2 (1.0%)
Grade 4 (<500/mm^3)	7 (3.4%)
G-CSF use	9 (4.4%)
Thrombocytopenia	
Grade 3 (20,000 – <50,000/mm^3)	10 (4.9%)
Grade 4 (<20,000/mm^3)	3 (1.5%)
Thrombopoïetin Use	2 (1.0%)

EPO: Erythropoïetin; G-CSF: granulocyte-colony stimulating factor

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Multivariate analysis: baseline predictors of severe complications*

Predictors	OR	95%CI	*P*-value
Platelet count ≤100,000/mm^3	3.11	1.32-7.73	0.0098
Serum albumin level <35 g/L	6.33	2.66-15.07	<0.0001

* Death, severe infection and hepatic decompensation, n=32 (6.4%)

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Multivariate analysis: baseline predictors of anemia <8g/dL or blood transfusion *

Predictors	OR	95%CI	*P*-value
Gender: Female	2.19	1.11-4.33	0.023
No lead-in phase	2.25	1.15-4.39	0.018
Age ≥65 years	3.04	1.54-6.02	0.0014
Hemoglobin level ≤12 g/dL for female ≤13 g/dL for male	5.30	2.49-11.25	<0.0001

* n=71 (14.3%)

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Preliminary conclusions

- In this large cohort of compensated cirrhotic patients, the safety profile of TVR or BOC in triple combination was poor as compared with phase III trials (Increased rates of SAEs and more difficult management of anemia) but associated with high rates of on-treatment virologic response
- Risk / benefit ratio should be assessed in cirrhotic experienced patients with platelets count ≤100,000/mm^3 or serum albumin level <35 g/L. These patients should be treated on a case by case basis due to high risk to develop severe complications
- However, cirrhotic experienced patients without predictors of severe complications should be treated but cautiously and carefully monitored

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