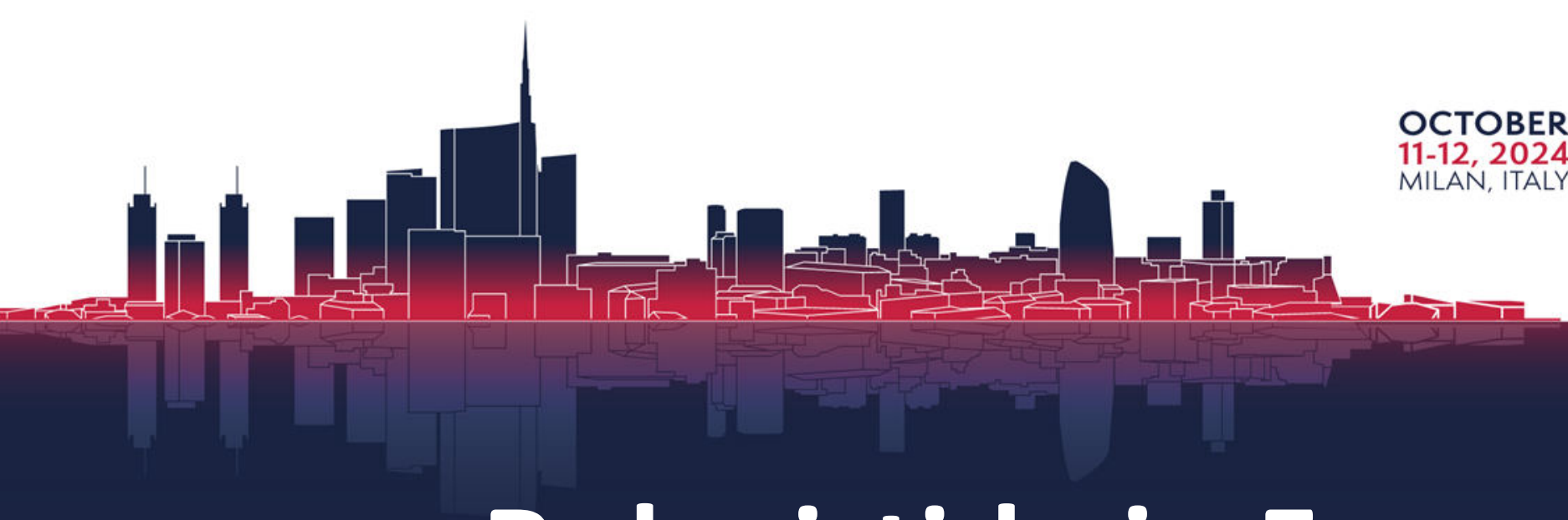


OCTOBER 11-12, 2024 MILAN, ITALY

DeltaCure 3rd International Meeting

Bulevirtide in France: multicenter study update

Dr H. Fontaine **on behalf ANRS HD EP01 BuleDelta study group**

Links of interest

- Employee of Gilead from October, 2022 to October, 2023.

Plan

ANRS French multicenter real-life cohort started in 2019

- Study progress

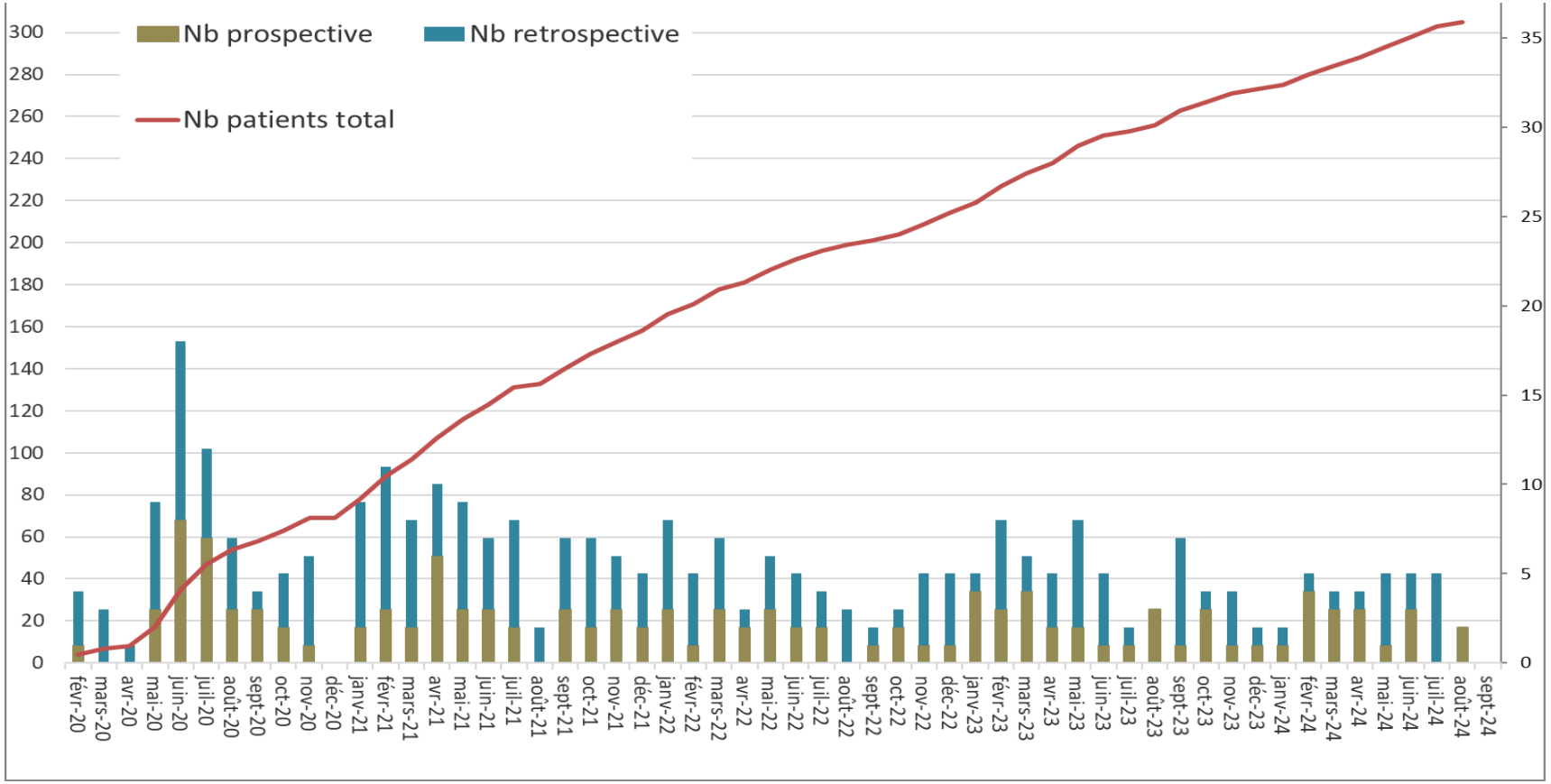
- Update of results:
  - Efficacy and safety of treatment with bulevirtide in HIV-infected patients
  - Sustained virological response after treatment with bulevirtide discontinuation
  - Effect of Peg-IFN on the viral kinetics of patients treated with bulevirtide according a mathematical model

- Perspectives

Study progress of the cohort

Inclusions

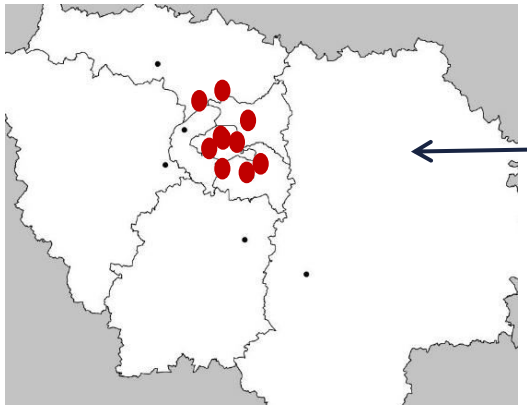
October 3, 2024: 311 patients = 127 prospectively and 184 retrospectively



5 patients/month

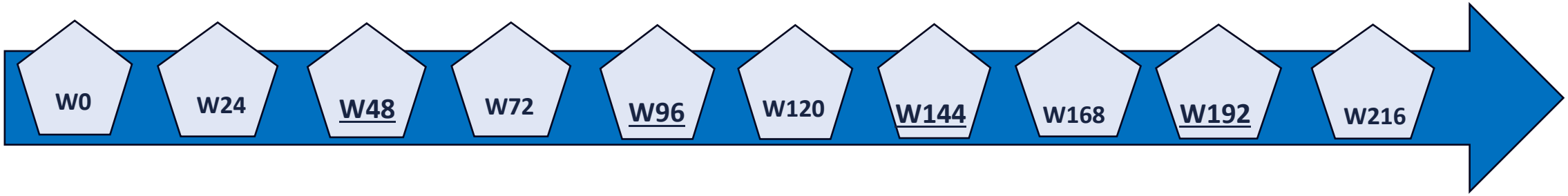
Multicenter study

37 investigator centers



Ile de France:
Avicennes
Beaujon
Bichat
Cochin
CH Créteil
Henri Mondor
La Pitié- Salpêtrière
Paul Brousse
Saint-Antoine
St-Louis-Lariboisière
Tenon

Patient number per visit



Patients	311	288	232	188	144	104	76	56	35	24

Characteristics of patients

Initial characteristics	N = 273
Age (years), mean ± SD	42.53 ± 11.00
Gender (M/F)	187/86
HIV coinfection, n (%)	37 (13.6%)
Cirrhosis, n (%)	215 (78.8%)
Fibroscan (kPa), mean ± SD	14.74 ± 9.79
Platelets (G/L), mean ± SD	148.35 ± 64.59
Bulevirtide duration (months), mean ± SD	19.42 ± 11.33
Treatment with interferon, n (%)	127 (46.7%)
HDV RNA log IU/mL, mean ± SD	6.08 ± 1.43
HDV genotype 1/5, n (%)	195 (97,9%)
HBV DNA log IU/mL, mean ± SD	2.27 ± 1.47
HBsAg (UI/ml) at inclusion	10,818.98 ± 25,134.52

Update of results

Specific population: HIV-infected patients (1)

Research article

JHEP|Reports

Treatment with bulevirtide in HIV-infected patients with chronic hepatitis D: ANRS HD EP01 BuleDelta and compassionate cohort

Victor de Lédinghen[1,*], Claire Fougerou-Leurent[2], Estelle Le Pabic[2], Stanislas Pol[3], Dulce Alfaiate[4], Karine Lacombe[5], Marie-Noëlle Hilleret[6], Caroline Lascoux-Combe[7], Anne Minello[8], Eric Billaud[9], Isabelle Rosa[10], Anne Gervais[11], Vlad Ratziu[12], Nathalie Ganne[13], Georges-Philippe Pageaux[14], Vincent Leroy[15], Véronique Loustaud-Ratti[16], Philippe Mathurin[17], Julie Chas[18], Caroline Jezequel[19], Sophie Métivier[20], Jérôme Dumortier[21], Jean-Pierre Arpurt[22], Tarik Asselah[23], Bruno Roche[24], Antonia Le Gruyer[25], Marc-Antoine Valantin[26], Caroline Scholtès[27], Emmanuel Gordien[28], Christelle Tual[2], Amel Kortebi[2], Fatoumata Coulibaly[29], Eric Rosenthal[29], Miroslava Subic-Levrero[30], Dominique Roulot[13], Fabien Zoulim[30], the ANRS HD EP01 BuleDelta study group

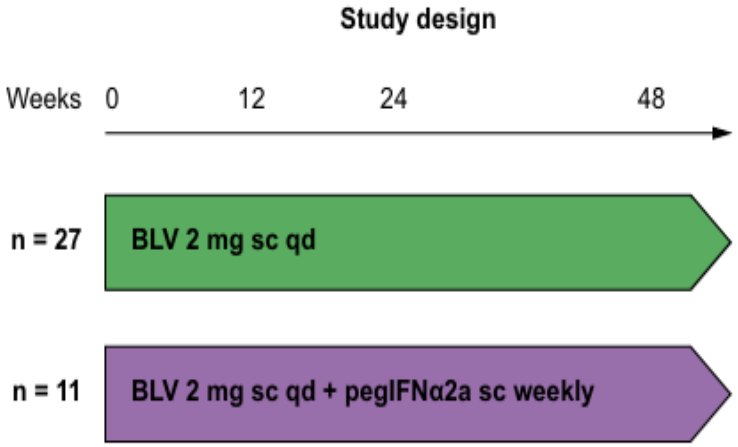
JHEP Reports **2024**. vol. 6 | 1–7

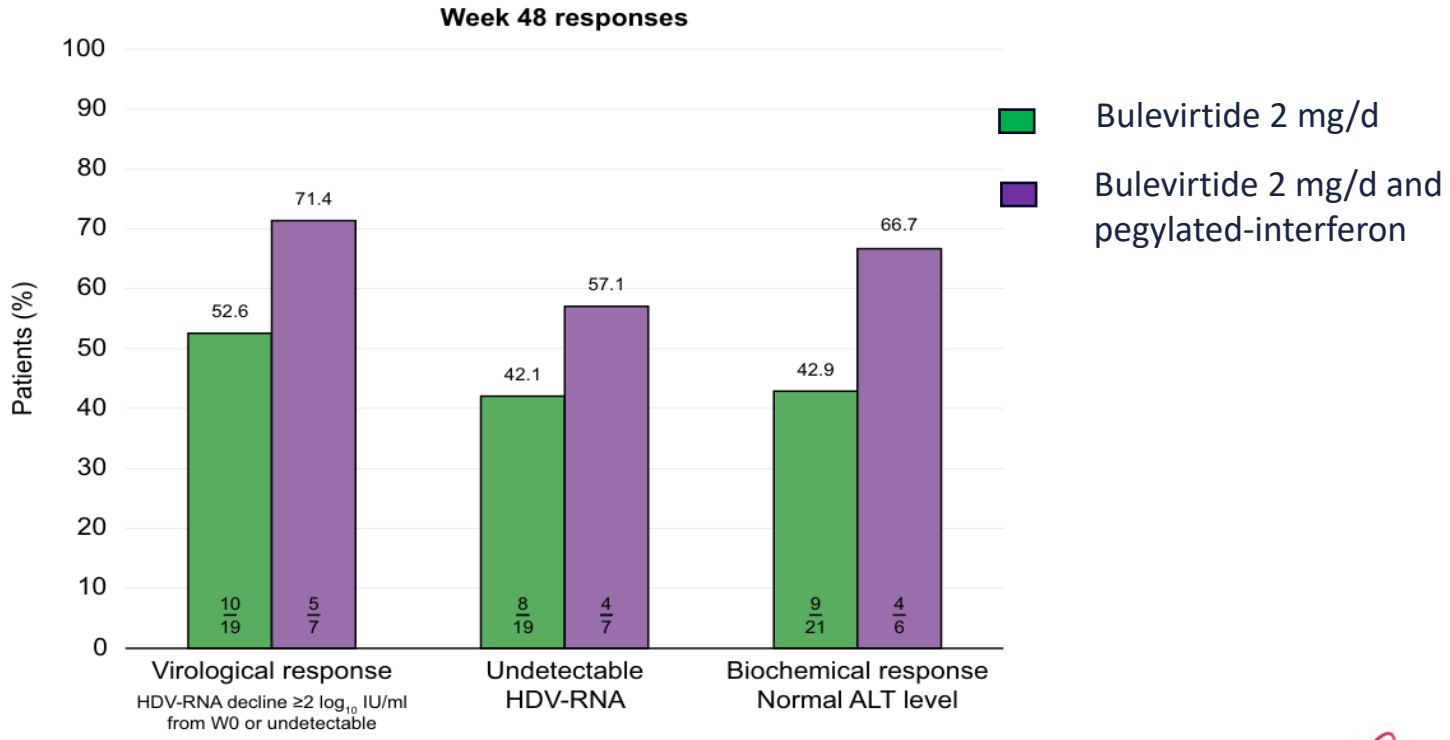
Check for updates

Specific population: HIV-infected patients (2)

Objectives: analyse the efficacy and the safety of treatment with bulevirtide associated or not with pegylated interferon in 38 HIV-infected patients (27 from Buledelta cohort and 11 from the compassionate use cohort)

Characteristics: 28 males, 47.7 ± 8.6 years, 68 % with cirrhosis, HDV RNA 5.7 ± 1.2 log10 UI/ml, HIV RNA 32 cp/mL and 566 CD4/mm3, median follow-up 83 (4-161) weeks, 97 % treated with analogs and 60 % undetectable HBV DNA





Conclusion

- In this first study analysing the efficacy and safety of treatment with bulevirtide (associated or not with pegylated interferon) in HIV-infected patients:

  - a virological response was observed in more than 50 % of patients at W48
  - with a fair tolerance and without specific drug-drug interactions (no impact on HIV replication and CD4 rate),

- Suggesting that bulevirtide should be considered as first-line therapy in HIV-HDV infected patients, with or without pegylated interferon as recommended by international current guidelines

Sustained virological response after treatment with Bulevirtide in HDV patients. Data from the French multicenter real-life cohort

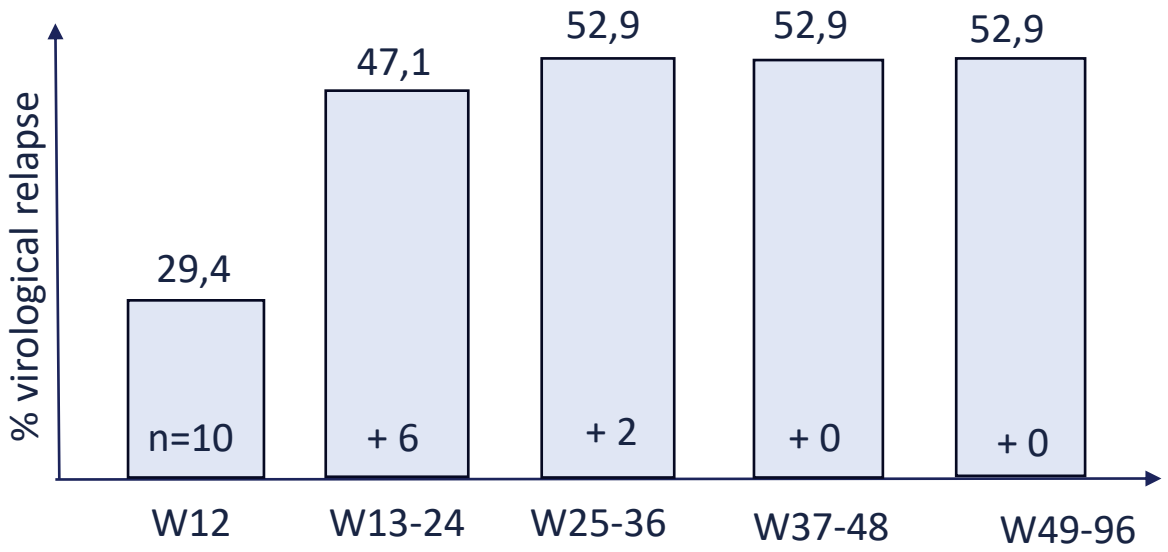
EASL June 2024

V. de Lédinghen[1], K. Lacombe[2], S. Pol[3], L. Alric[4], C. Lascoux-Combe[5], D. Alfaiate[6], M.N. Hilleret[7], N. Ganne[8], J. Gournay[9], V. Loustaud-Ratti[10], **M. Subic-Levrero[6]**, F. Coulibaly[11], E. Le Pabic[12], C. Tual[12], S. Brichler[13], F. Zoulim[11]

Sustained virological response (2)

Objective: evaluate the prevalence and the factors associated with sustained virological response (SVR) in 34 patients treated with BLV (22 with and 12 without PEG-IFN) and with undetectable or unquantifiable HDV RNA at the end of therapy

Characteristics: 50 % males, 44 years, 77 % with cirrhosis, 21 % HIV-infection, HDV RNA 5,8 log10 IU/mL, median follow-up 18 ± 9 months



Conclusion:

- At W96, sustained virologic response : 47,1 %
- 18 relapses including 88,9 % in the first 24 weeks of follow-up
- No factor was identified to be associated with SVR

HDV kinetics during Bulevirtide treatment (1)

Effect of Peg-IFN on the viral kinetics of patients with HDV infection treated with bulevirtide

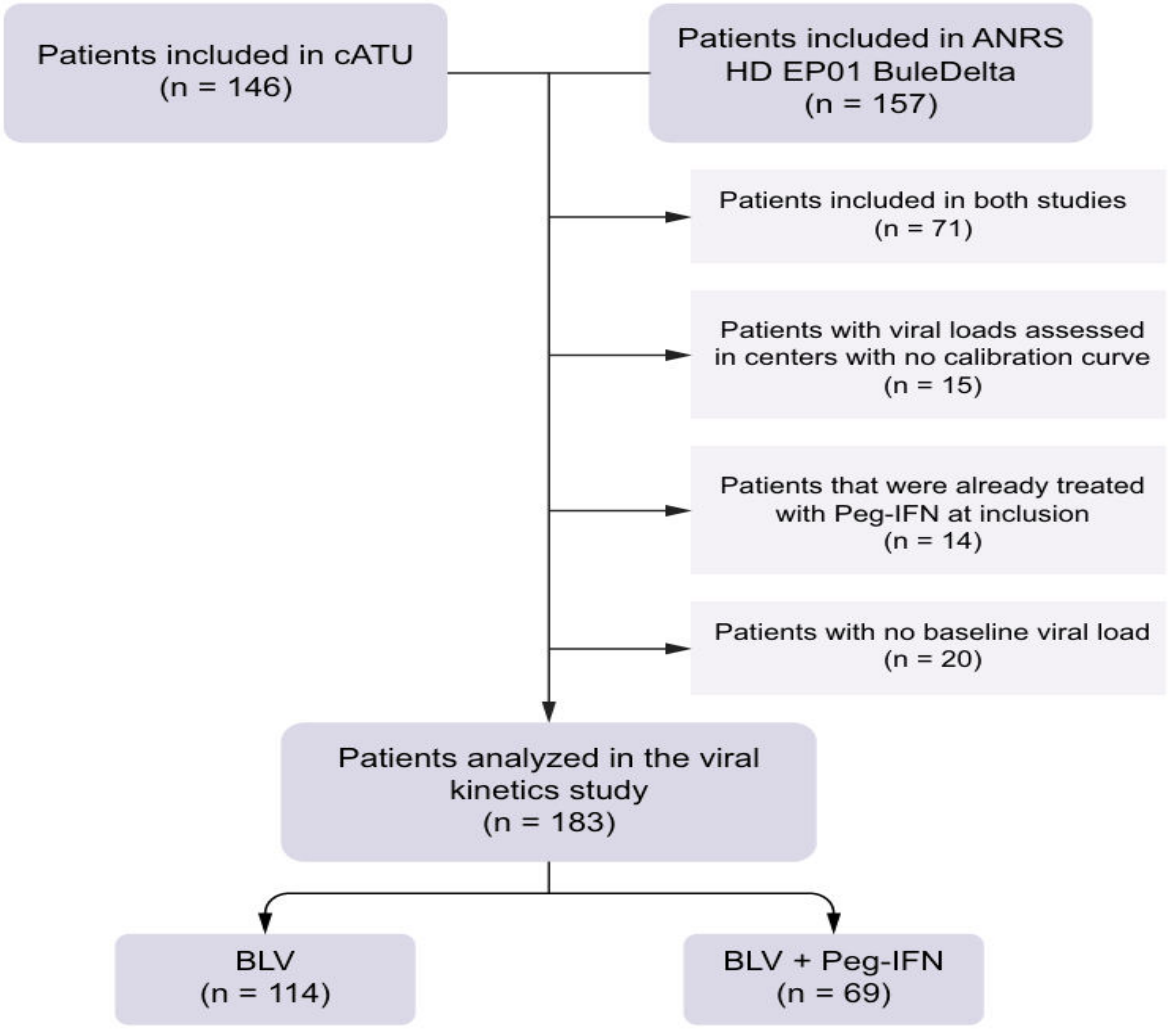
Selma El Messaoudi,[1,*] Ségolène Brichler,[2] Claire Fougerou-Leurent,[3,4] Emmanuel Gordien,[2] Athenaïs Gerber,[2] Amal Kortebi,[3,4] Garance Lagadic,[3,4] Miroslava Subic-Levrero,[5] Sophie Metivier,[6] Stanislas Pol,[7] Anne Minello,[8] Vlad Ratziu,[9] Vincent Leroy,[10] Philippe Mathurin,[11] Laurent Alric,[12] Fatoumata Coulibaly,[13] Jean-Michel Pawlotsky,[14] Fabien Zoulim,[5] Victor de Lédinghen,[15,†] Jérémie Guedj [1,†], the ANRS HD EP01 BULEDELTA Study Group

JHEP Reports **2024.** https://doi.org/10.1016/j.jhepr.2024.101070

HDV kinetics during Bulevirtide treatment (2)

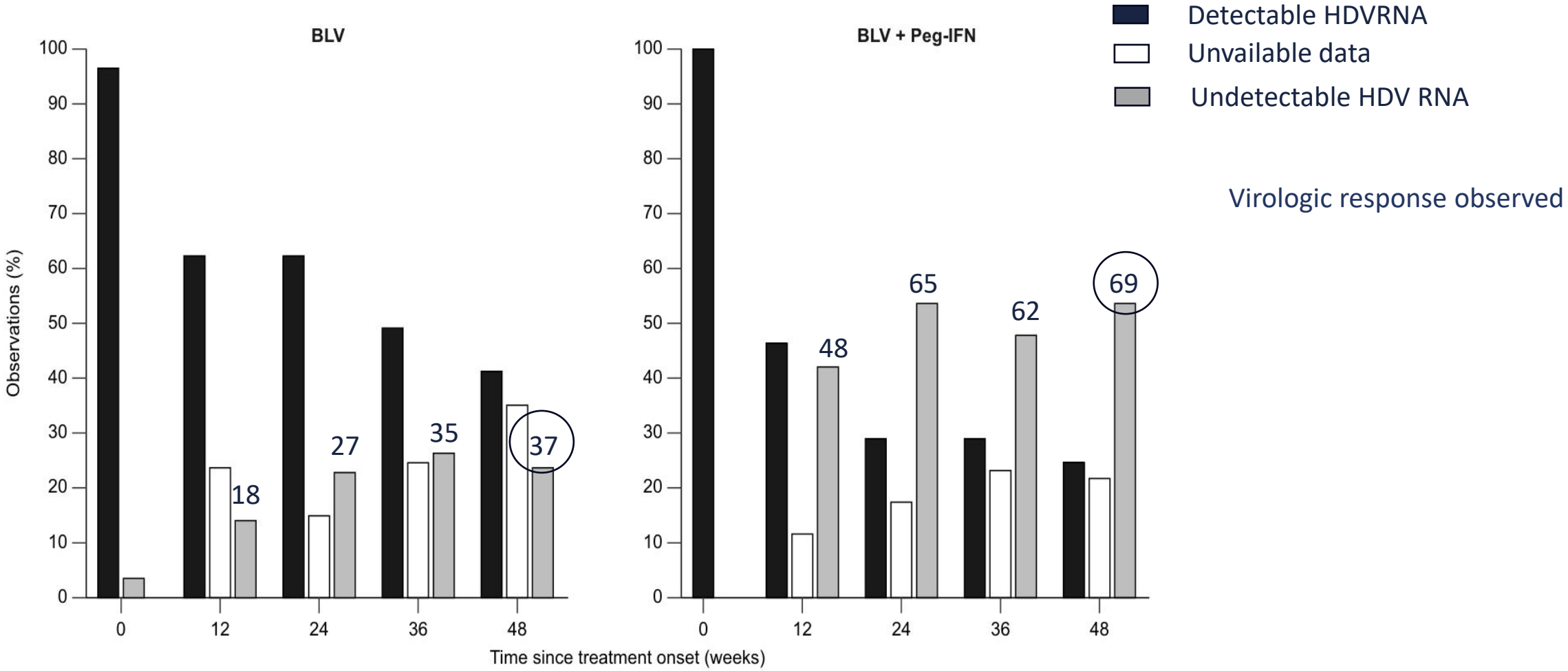
Objectif : analyze of the viral kinetics of Hepatitis D virus, using a mathematical modelling, in 183 patients treated with Bulevirtide (69 with and 114 without pegylated interferon)

Characteristics : 68 % males, 42 years, 74 % cirrhosis, 17 % HIV infection, HDV RNA 6,6 $\log_{10}$ IU/mL, median follow-up of 338 days



HDV kinetics during Bulevirtide treatment (3)

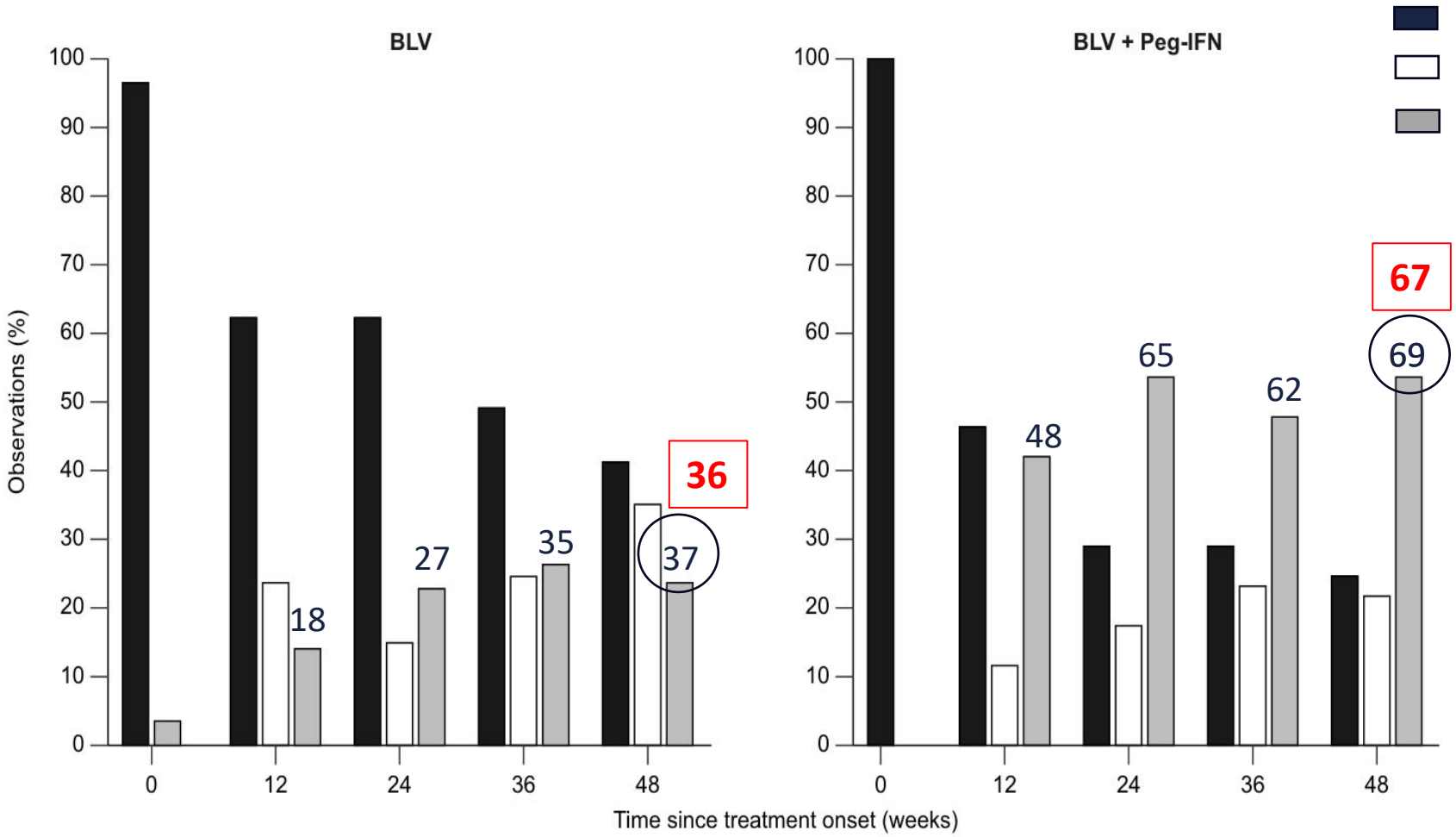
Virologic response



Virologic response observed

HDV kinetics during Bulevirtide treatment (3)

Virologic response

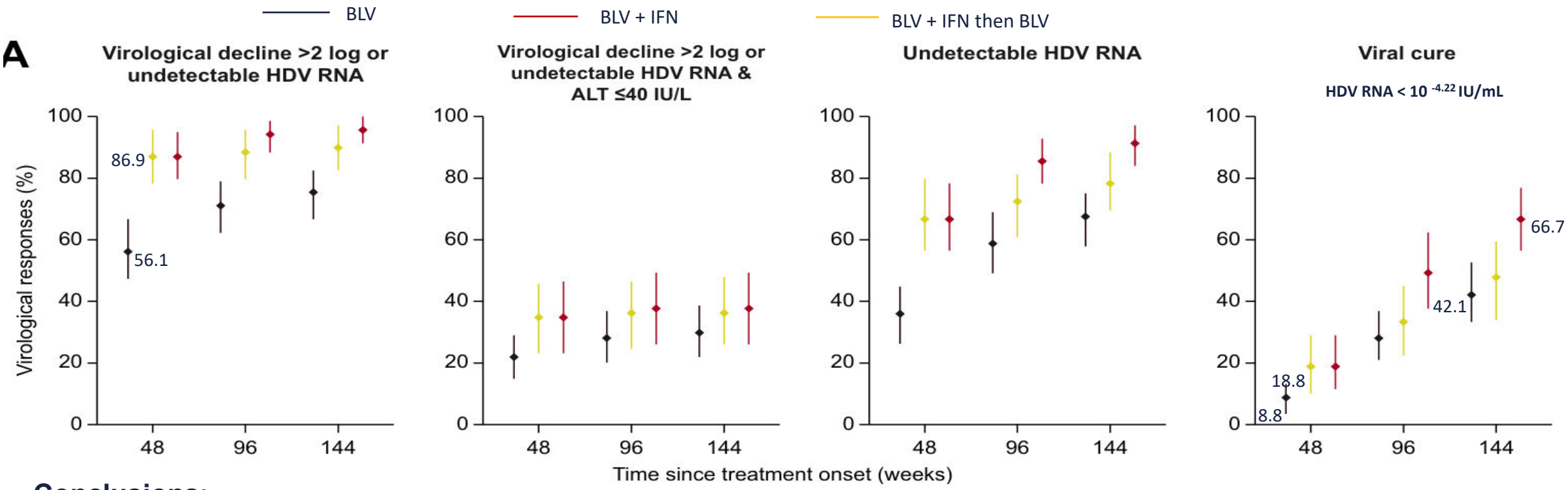


Virologic response observed

Virologic response predicted

At W 96, virological response predicted vs observed :
-in BLV patients: 60 vs 55 %
-in BLV + IFN patients: 83 vs 72 %

HDV kinetics during Bulevirtide treatment (4)



Conclusions:

- The use of mathematical models shows that BLV block cell infection, with a large inter-patient variability
- The addition of Peg-IFN strongly enhances viral kinetics, with a predicted HDV cure more frequent with the Peg-IFN association than BLV monotherapy. The long-term benefit of therapeutic association has to be proven by clinical trials

Accepted for communications

Delta Cure: Detection and characterization of anti-preS1 antibodies in HDV-infected patients under Bulevirtide treatment.

Aronthippaitoon Y, Szerman. N, Roch E, Zoulim F, Sureau C, Gaudy-Graffin C, and the ANRS HDEP01 Buldelta study group.

AASLD: Second line treatment with bulevirtide in HDV patients from the ANRS-MIE French multicenter real-life cohort ANRS HD EP01 BULEDELTA - Subic M et al

Perspectives : in 2025

ANRS HD EP 01 BuleDelta

=> ANRS HD EP 01 HepDelta

BuleDelta => HepDelta

- **Modifications of inclusion criteria :**
  - All HVD patients, treated or not
  - All patients treated, whatever the treatment

- **Modifications of objectives :**
  - Natural history without treatment (clinical, virological, biochemical and histological data)
  - Comparison between untreated and treated patients
  - Identification of factors associated with
    - -severe liver disease, with clinical liver-related events
    - -virological, biochemical and combined response
    - -sustained virological response (baseline characteristics, treatment, duration of undetectability before discontinuation),
  - Impact of the therapeutic response on global and liver-related morbidity and mortality

- **Modification of prevised effective of patients** : 400 => 800

- **Extension of follow-up and changes in monitoring** patients according the therapeutic status (biobank, survey)

Thank you for your attention

Thank to the patients and to all the BuleDelta team