



# Retreatment of DAA failures with approved regimens and resistance information in a real life setting: data from the Gehep004 cohort

AB Perez & F García

HOSPITAL UNIVERSITARIO SAN CECILIO

 **ibs.GRANADA**  
INSTITUTO DE INVESTIGACIÓN BIOSANITARIA



# Disclosures

---



- Lectures, advisory boards from:
  - Abbvie, Gilead, Roche, MSD, ViiV
- Employee from Servicio Andaluz de Salud
- Grant from Abbvie to attend this meeting

# Background

---



- Growing evidence on the need to use resistance testing to guide retreatment
- Also for baseline in GT1a & 3, to guide treatment duration and/or the need to use Ribavirine
- Retreatments data come mainly from clinical trials
- Information from “Real life” is scarce and is of high clinical value
- Spain DAA rollout, from SOF/SIM to SOF/VEL

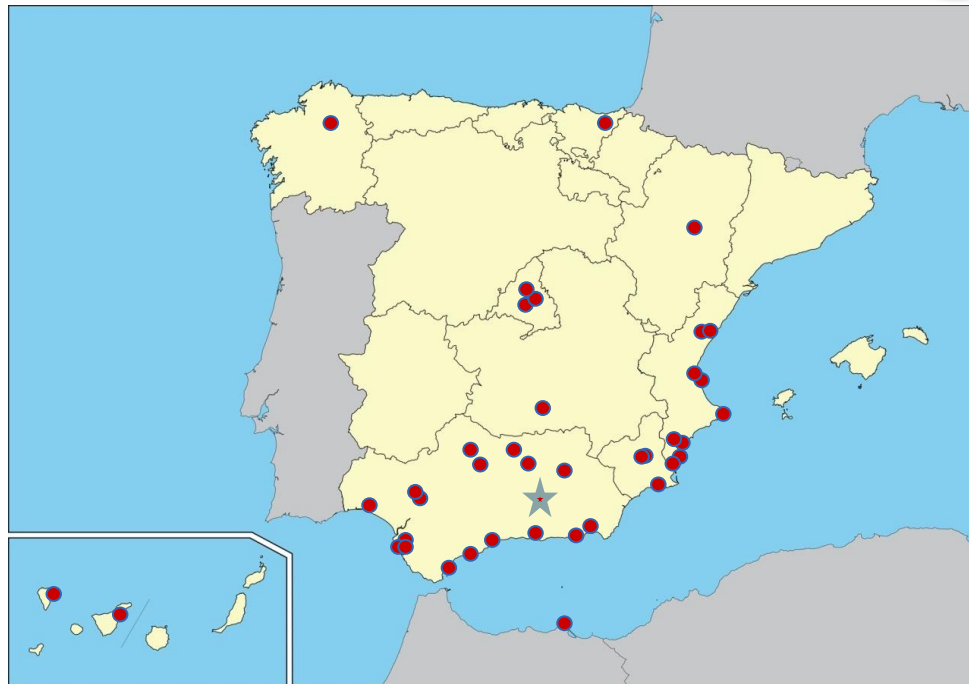
# GEHEP-004 Cohort



- 54 centers from Spain
- Running since 01/16
- Updates  $\pm$  6 months

**7189** patients

**289** VF



Last Update: **December 2016**

# Aim

---



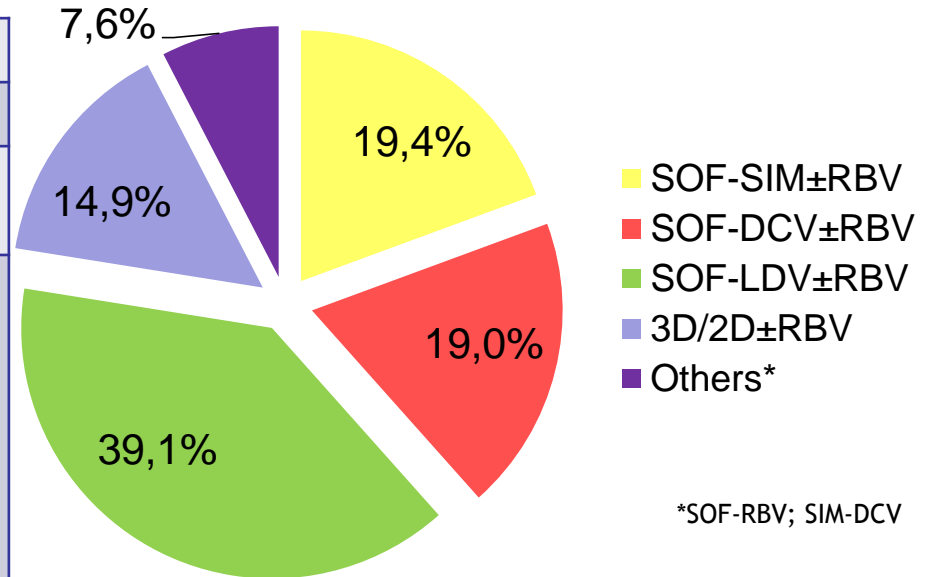
- To evaluate:
  - the prevalence of HCV resistance associated substitutions (RAS)
  - how patients are being retreated,
  - the efficacy of retreatment regimens,
  - and how retreatment has adhered to treatment guidelines recommendations and resistance findings.

# GEHEP-004 resistance

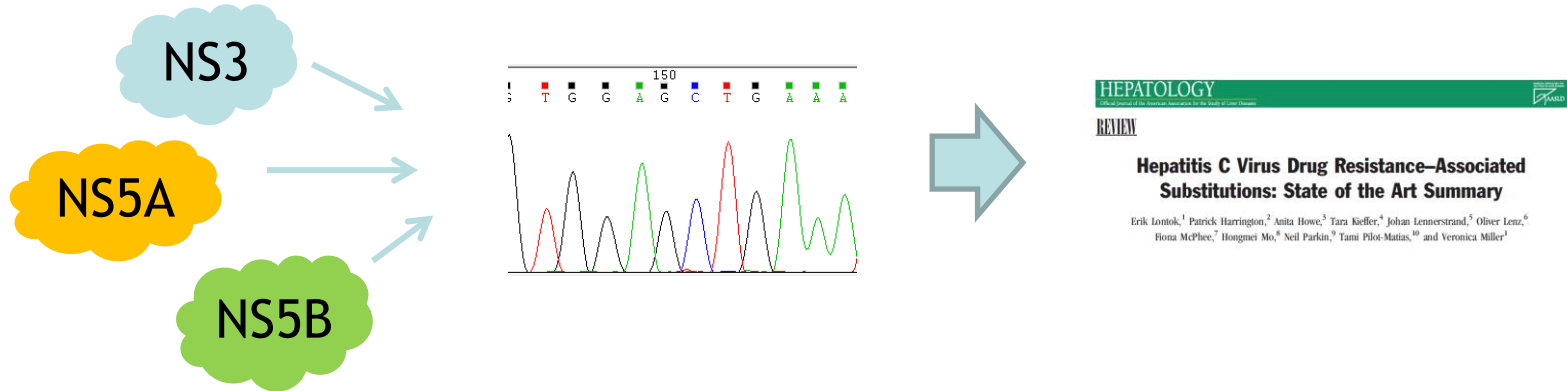


- **289 patients** evaluated for DR

Sex	84.8% male
Age (years)	53, IQR 48-58
VIRAL LOAD (Log UI/ml)	5.91, IQR 5,41-6,41
GENOTYPE (at origin)	HCV-1 (8) HCV-1A (86) HCV-1B (84) HCV-2 (1) HCV-3/3a (54) HCV 4 or 4a/c/d (47) OTHER [mixed infection] (2) Unkown(7)



# Methods

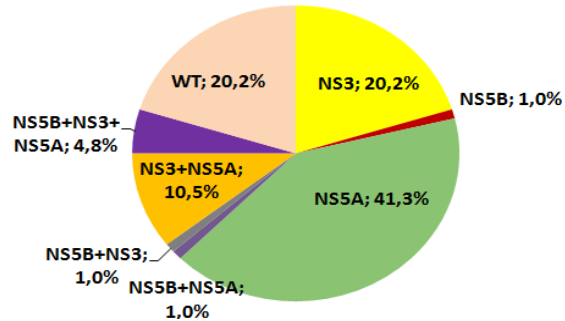


- **NGS** to study mixed infections & reinfections
- NS5B (NS3, NS5A) sequence was also used for genotype assignment

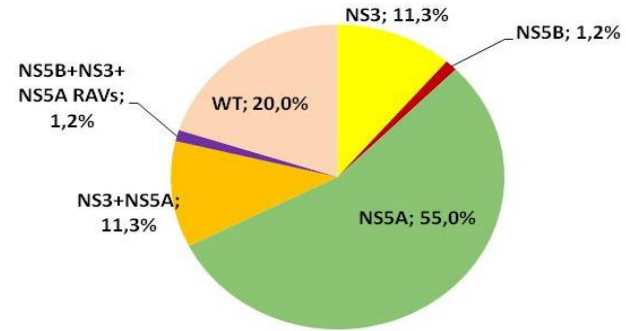
# RAS detection by genotype



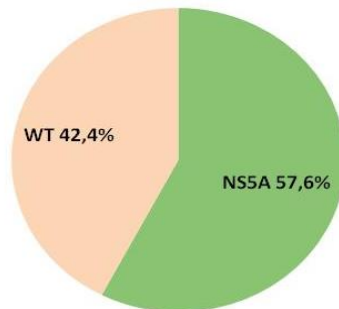
## Genotype 1a (n=104)



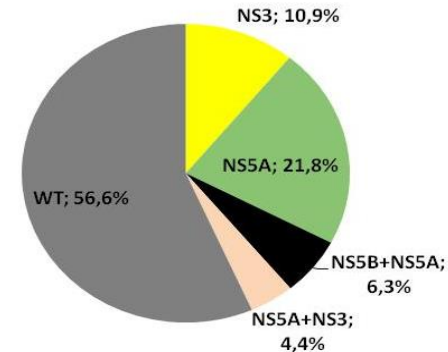
## Genotype 1b (n=80)



## Genotype 3 (n=59)



## Genotype 4 (n=46)

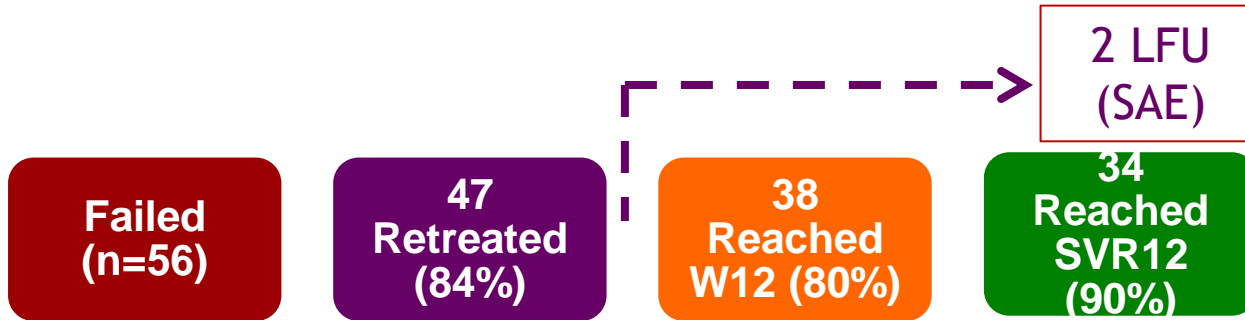




# Sofosbuvir+Simeprevir±RBV



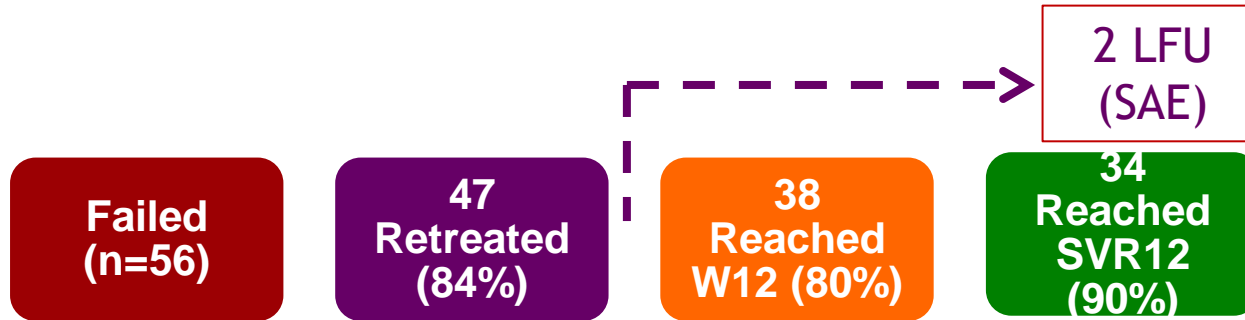
- 59 % had RASs in NS3; 5.4% in NS5A



# Sofosbuvir+Simeprevir±RBV



- 59 % had RASs in NS3; 5.4% in NS5A



Genotype	Retreatment Regimen	SVR 12, % (n/N)
1a (79)	• SOF-LDV±RBV 12/24w	92 (12/13)
1b (57)	• SOF-LDV±RBV 12/24w	86 (12/14)
	• SOF-DCV 24w	0 (0/1)
4 (39)	• SOF-LDV±RBV 12/24w	100 (9/9)

# Sofosbuvir+Simeprevir±RBV



- Second line failures

GT	Cirrhosis	TE (IFN)	Duration/ RBV	Retreatment	NS5A RASs	Others
1a	No	N.D.	12w	SOF-LDV 24s	No	Kidney & Liver Trasplant
1b	Yes	Yes	12w/RBV	SOF-DCV 24s	No	HCC
1b	Yes	Yes	12w	SOF-LDV 24s	No	-
1b	Yes	Yes	ND	SOF-LDV 24s	L31M	HCC

# Sofosbuvir+Daclatasvir±RBV



- 80 % had RASs



# Sofosbuvir+Daclatasvir±RBV



- 80 % had RASs



Genotype	Retreatment Regimen	SVR 12, % (n/N)
1 1a (85) 1b (100)	<ul style="list-style-type: none"> <li>SOF-SIM-RBV 24w</li> <li>SOF-LDV±RBV 12/24w</li> <li>3D±RBV 12/24w</li> <li>SOF-3D-RBV 24w</li> </ul>	67 (2/3) 33 (1/3) 100 (2/2) 100 (1/1)
3 (72)	<ul style="list-style-type: none"> <li>SOF-DCV-RBV 24w</li> <li>SOF-LDV±RBV 24w</li> <li>SOF-RBV 24w</li> <li>PegINT-SOF-RBV 12w</li> </ul>	100 (2/2) 100 (2/2) 50 (1/2) 100 (1/1)
4 (50)	<ul style="list-style-type: none"> <li>2D±RBV 12/24s</li> </ul>	50 (1/2)

# Sofosbuvir+Daclatasvir±RBV



- Second line failures

GT	Cirrhosis	TE (IFN)	Duration/ RBV	Retreatment	NS5A RASs	Others
1a	Yes	N.D.	24w	SOF-SIM-RBV 24w	M28T+Q30H	HIV
1a	Yes	No	12w	SOF-LDV-RBV 24w	L31M	-
1b	No	Yes	12w	SOF-LDV 12w	L31IMV Y93H	-
3a	Yes	Yes	24w	SOF-RBV 24w	Y93H	HIV
4a	No	No	12w	2D 12w	L30H	Liver Transplant. GT error 3a

# Sofosbuvir+Ledipasvir±RBV



- 83 % had RASs

**Failed  
(n=113)**

**54  
Retreated  
(48%)**

**32  
Reached  
W12 (59%)**

**18  
Reached  
SVR12  
(88%)**

# Sofosbuvir+Ledipasvir±RBV



- 83 % had RASs

**Failed  
(n=113)**

**54  
Retreated  
(48%)**

**32  
Reached  
W12 (59%)**

**18  
Reached  
SVR12  
(88%)**

Genotype	Retreatment Regimen	SVR 12, % (n/N)
1a (70)	• SOF-SIM-RBV 12/24w	80 (4/5)
	• SOF-LDV-RBV 12/24w	75 (3/4)
	• 3D-RBV 12/24w	100 (2/2)
1b (97)	• SOF-SIM±RBV 12/24w	100 (9/9)
	• SOF-LDV-RBV 24w	100 (1/1)
	• 3D-RBV 12w	100 (1/1)
3 (6)	• SOF-DCV-RBV 12/24w	80 (4/5)
4 (38)	• SOF-SIM-RBV 24w	100 (2/2)
	• SOF-DCV-RBV 24w	100 (1/1)
	• 2D-RBV 12w	50 (1/2)



# Sofosbuvir+Ledipasvir±RBV



- Second line failures

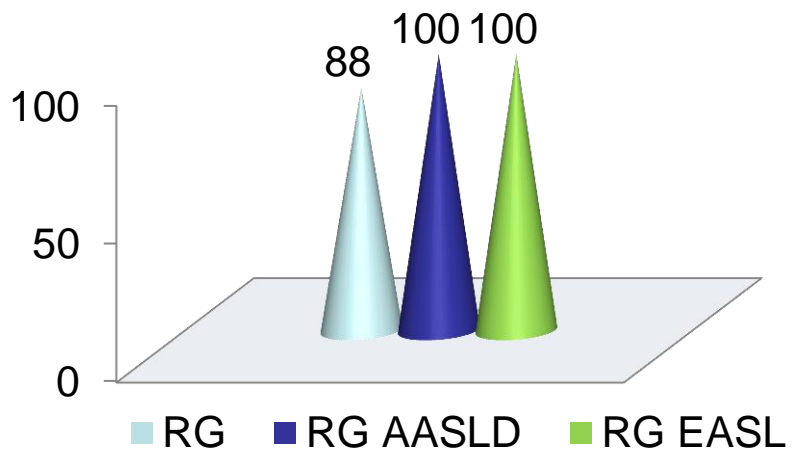
<b>GT</b>	<b>Cirrhosis</b>	<b>TE (IFN)</b>	<b>Duration/ RBV</b>	<b>Retreatment</b>	<b>NS5/NS3 RASs</b>	<b>Others</b>
1a	No	N.D.	8w	SOF-SIM-RBV 12w	No/-	HIV
1a	Yes	Yes	12w	SOF-LDV-RBV 24w	No	HIV
3a	Yes	No	24w	SOF-DCV-RBV 24w	No	-
4d	No	Yes	12w	2D-RBV 12w	No	HIV

# Retreatment regimen & efficacy

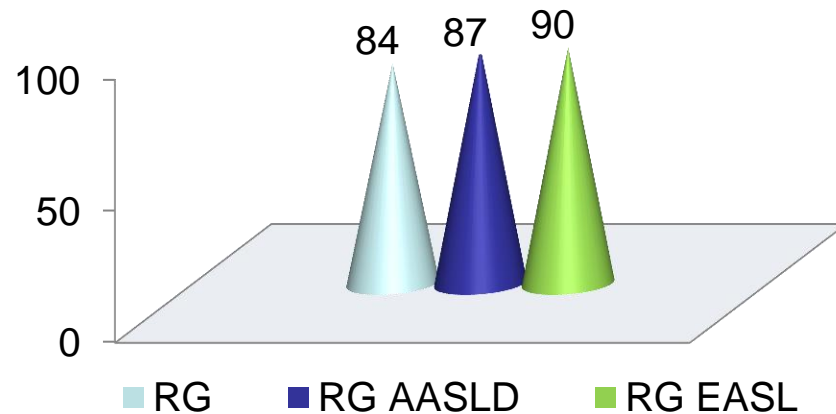


	<b>SOF-SIM±RBV</b>	<b>SOF-LDV±RBV</b>	<b>SOF-DCV±RBV</b>	<b>3D/2D±RBV</b>
Failed ( n )	56	113	55	43
With RASs (%)	59% (NS3)	65% NS5A 3% S282T	80% NS5A	69% NS5A 37% NS3 14% ALL
Retreated (n)	47	54	25	14
Reached W12 (n)	38	32	18	3
Reached SVR12	34 90%	28 88%	13 72%	2 66%

# Resistance & Guidelines



SOF-Simeprevir (n=40)



SOF-Ledipasvir (n=29)

# Conclusions

---



- Genotype 1a, 1b & 3 patients failing DAAs in Spain harbor a high prevalence of RASs, especially if they are failing approved NS5A containing combinations
- Genotype 3 patients failing SOF/LDV are less prone to develop NS5A RASs than SOF/DCV failures.

# Conclusions

---



- Patients failing first line regimens in Spain have been in general successfully retreated with the available combinations.
- Resistance testing has helped to the success in retreatment in patients who have failed a first line, especially when accompanied with recommendations on treatment duration and on the need to use ribavirine.

# Acknowledgments



The study has been funded by Plan Nacional de I+D+I, ISCIII-Subdirección General de Evaluación, Fondo Europeo de Desarrollo Regional (FEDER), PI15-00713, Consejería de Salud, Junta de Andalucía (PI/0411.2014) & II Conv Nacional de Proyectos GEHEP

# Acknowledgments



- Complejo Hospitalario de Jaén: M Omar
- Complejo Hospitalario Santiago Compostela: A Aguilera
- CP Albolote: JJ Antón
- CP Castellón: C Mínguez
- CP Córdoba: J De Juan
- EPHAG Andújar: C Delgado
- Hospital Arnau de Vilanova: J Flores
- Hospital Carlos Haya: M Jiménez, M Delgado
- Hospital Cartagena: F Vera, O Martínez
- Hospital Comarcal de la Vega Baja: R Sáez
- Hospital Costa del Sol: JM Rosales; N Montiel
- Hospital de Baza: J Guilarte
- Hospital de Denia: P Martín, MD Marco
- Hospital de Elche: M Masiá, F Gutierrez
- Hospital de Fuenlabrada: I García-Arata
- Hospital de Jerez: JC Alados
- Hospital de La Línea: F Téllez
- Hospital de La Palma: M Vélez, L Martín
- Hospital de Montilla: M Chicano
- Hospital de Poniente: M Álvarez, E Fuertes, A Lozano
- Hospital de Puerto Real: F Téllez, JM Montero
- Hospital de Sagunto: J Primo
- Hospital de Valdepeñas: P Reales
- Hospital de Vinalopó: V Navarro, L Giner
- Hospital General de Alicante: S Reus, J Portilla, L Giner
- Hospital General de Valencia: M Diago, M Garcia-delToro, MD Ocete
- Hospital General JM Morales Meseguer: P Antequera
- Hospital Gregorio Marañón: T Aldamiz-Echevarría, E Reigadas, R Alonso
- Hospital Infanta Elena: A de la Iglesia, D Merino
- Hospital Juan Ramón Jiménez: F.M. Jiménez
- Hospital La Princesa: L Cardeñoso, I Santos
- Hospital Marina Baja: A García
- Hospital Melilla: A Fernández
- Hospital Miguel Servet: A Martínez-Sapiña, MA Simón
- Hospital Ntra. Sra. De la Candelaria: M Lara
- Hospital Puerta del Mar: Clotilde Fernández
- Hospital Punta de Europa: B Becerril
- Hospital Ramón y Cajal: MJ Vivancos, S Del Campo
- Hospital Reina Sofía de Córdoba: A Poyatos, A Rivero
- Hospital Reina Sofía de Murcia: E Bernal, A Alcaraz
- Hospital Torrecárdenas: A Collado, MC Galvez, M Gonzalez, M Casado
- Hospital Universitario de Donostia: MA von-Wichmann, J Arenas
- Hospital Universitario de La Plana: O Pérez
- Hospital Universitario de Torre Vieja: R Hernández
- Hospital Universitario La Paz: J González, S G. Bujalance, V Hontanón, R Micán
- Hospital Universitario San Carlos: MJ Téllez
- Hospital Universitario San Cecilio: J Salmerón, A Gila, E Ruiz Escolano, J Hernández-Quero, R Quiles
- Hospital Universitario Virgen de la Arrixaca: C Galera
- Hospital Virgen de la Victoria: J Santos
- Hospital Virgen de las Nieves: F Nogueras, M.A. López Garrido, S Espinosa
- Hospital Virgen de Valme: JA Pineda, E Suarez, S Bernal
- Hospital Virgen del Rocío: JM Pascasio, P Viciana
- Hospital Virgen Macarena: Felipe Fernández



**Gracias/Thank you**

**[abperezj@msn.com](mailto:abperezj@msn.com); [fegarcia@ugr.es](mailto:fegarcia@ugr.es)**