5th HEPATITIS C TECHNICAL ADVISORY GROUP

TAG Meeting

EVALUATION OF THE DIAGNOSTIC PERFORMANCE OF HCVcAg AS TEST OF CURE IN FOR HEPATITIS C AMONG PWID IN GEORGIA

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Outline

- Objectives
- Methods
- Results
- Limitations
- Conclusions

Objectives

- Evaluation of the performance of HCVcAg assay in confirming sustained virological response (SVR) at 12 weeks after treatment completion

- Estimation of sensitivity and specificity of HCVcAg in confirming SVR at 12 weeks after the end of treatment, measured against reference test (Abbott RealTi*me* HCV VL assay)

Study design

- Retrospective study
  - Archived leftover samples collected in 2015-2018 in Georgia as a part of routine clinical visit to test treatment outcome (SVR testing)
  - Archived leftover samples collected in 2015-2018 in Georgia subjects treated with first generation of DAA (sometimes association with interferon)
  - Tested for the presence of HCV RNA

- Study population:
  - “SVR + group”: documented detectable HCV RNA levels at 12 weeks after treatment completion
  - “SVR – group”: documented non-detectable HCV RNA at 12 weeks after treatment completion

Random sampling methodology

- Samples were selected randomly from a list of 4210 records available in the Neolab clinic database.
- The samples are stored frozen in block of 500 samples per block.
- The storing in each block is defined by the sample ID, several samples for each patients are stored corresponding to the stage of the diagnostics or treatment monitoring.
- According to the sample size of the study (maximum 300 for both groups), all samples positive at 12 week SVR were selected from each blocks and added randomly selected SVR negative samples to make 35 samples in average per block (average number of sample positive at SVR12 per block).
- The exception from this rule was for the last block, which did not reach 500 samples at that moment. The block was used to complete the planned number of negatives (n=150).

Samples inclusion and exclusion criteria

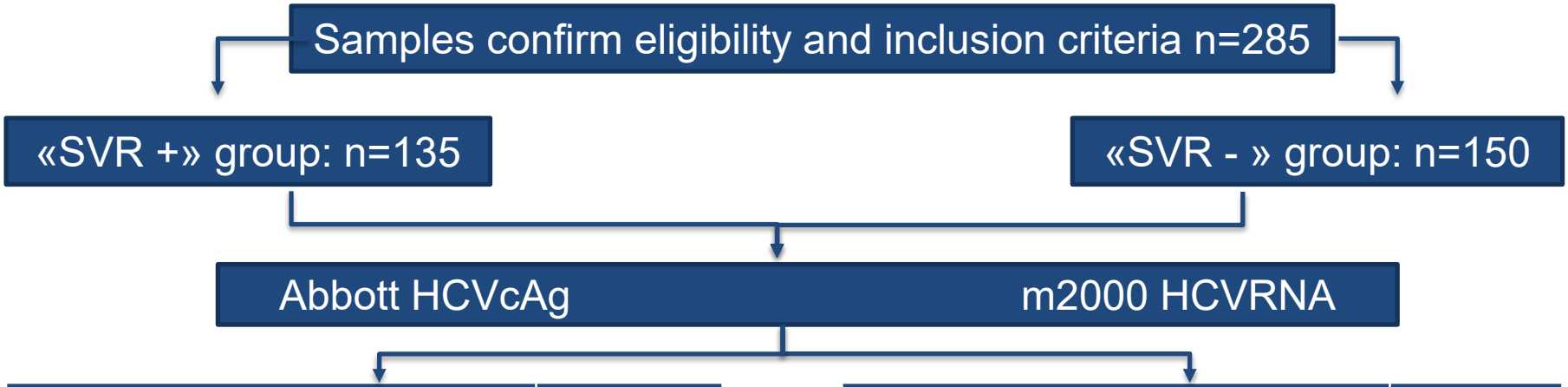
- Inclusion Criteria
  - Sample collected at 12 weeks after treatment completion
  - Sample has associated documented results of HCV RNA test approved for clinical use in Georgia
  - Sample volume is sufficient to perform index and reference testing as defined by the protocol (≥600 µl)
  - Sample has been stored according to GLP
- Exclusion Criteria
  - Sample are excluded from the study if any of the following exclusion criterion apply:
    - Samples had more than two freeze/thawing cycles

Population characteristics (n = 285)

Characteristics		N (%)
Age, median		48 (±8)
Gender	*Male*	246 (86)
	Female	25 (9)
	Unknown	14 (5)
HBsAg		5 (2)
Anti HBs		53 (19)
HIV		0 (0)
HCV genotype	*1*	97 (34)
	2	71 (25)
	3	108 (39)
	Multi-genotypes	9 (3)

Characteristics		N (%)
History of injecting drug	*currently*	2 (1)
	In the past	115 (40)
	no	123 (43)
	unknown	45 (16)
Fibroscan® liver disease stage	*F0-1*	13 (5)
	F2	11 (4)
	F3	52 (18)
	F4	100 (35)
	unknown	109 (38)
Treatment	*Interferon based*	124 (44)
	Harvoni	34 (12)
	Harvoni + ribavirin	67 (24)
	Triple therapy	60 (21)

Sample flow



HCVcAg	#
Non-Reactive	148
Reactive	125
Gz-Reactive (3-10 fmol/L)	9
error	4
Total	**282**

HCV RNA	#
Non-detected	86
Detected	100
Insufficient volume	73
error	27
Total	**186**

Result for both HCVcAg & HCV RNA **n=185**

Results for HCVcAg vs RNA at SVR12

		*m*2000 HCV RNA		
		Pos	Neg	Total
HCVcAg	Pos	82	0	87
	Gz-pos	5*	0	
	Neg	12**	86	98
	Total	99	86	185

*Sample HCVcAg Gz-reactive RNA level (IU/mL)
<30
32
246
339
725

**Sample HCVcAg non-reactive RNA level (IU/ml)
<30 (n=10)
200
515

Limitations

- Cryoprecepitates in the thawing plasma caused decreased volume or errors which decreased the samples size.

Conclusion

- Reactive HCVcAg tests at SVR12 confirm treatment failure (SVR12-HCV RNA+) with 100% specificity

- HCVcAg testing could miss low RNA VL (<30 IU/ml) samples of treatment failure

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