HCV
TREATMENT NAÏVE PATIENTS

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NO DISCLOSURES PERTAINING TO THIS PRESENTATION

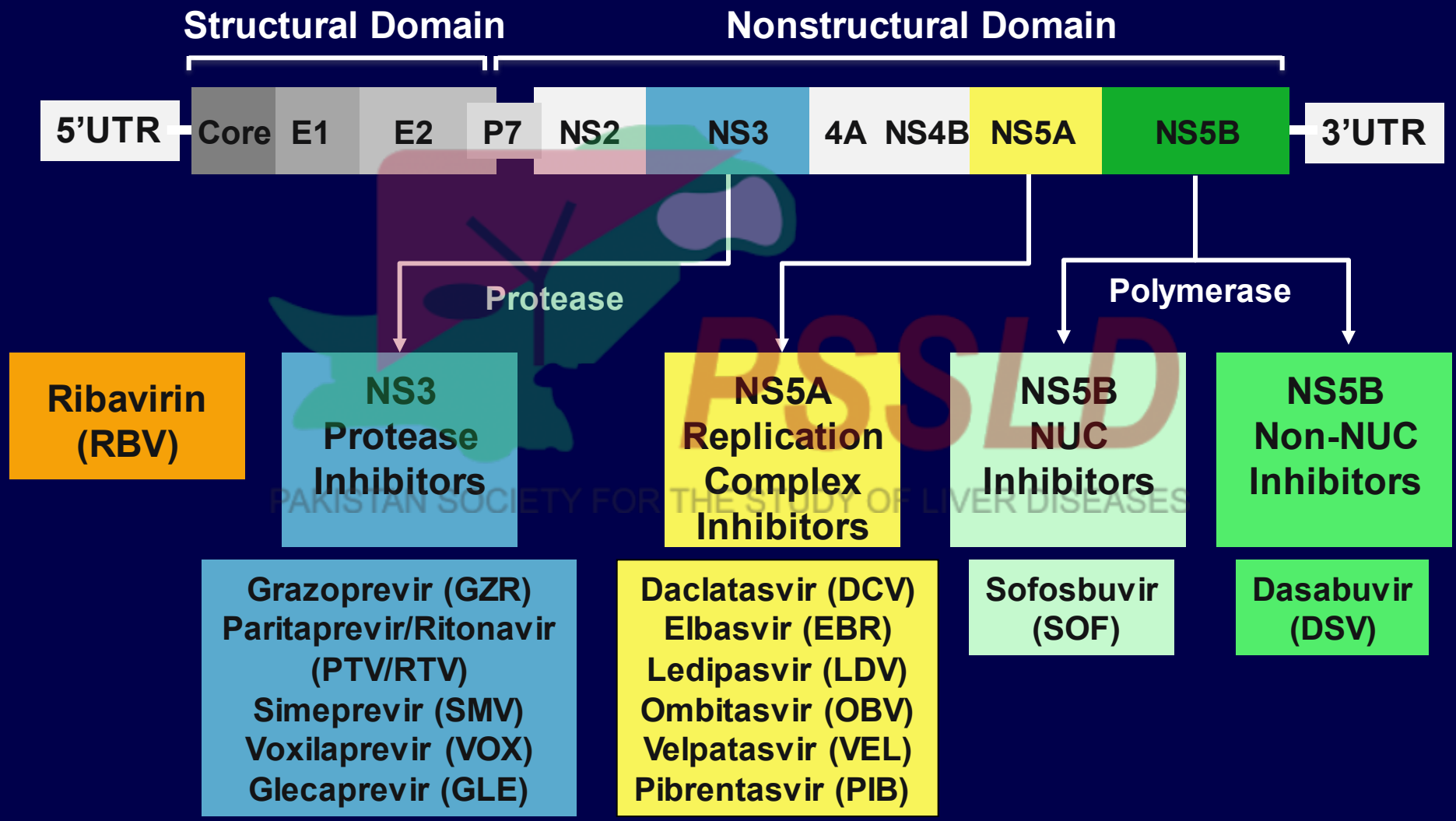
HCV DISEASE STAGES

- ACUTE HEPATITIS
- CHRONIC HEPATITIS
  - WITHOUT SIGNIFICANT FIBROSIS
  - WITH SIGNIFICANT FIBROSIS
    - BUT NO DECOMPENSATION
    - WITH DECOMPENSATION
    - WITH COMPLICATIONS

ALL HCV PATIENTS ABOVE THE AGE OF 12 ARE CANDIDATES FOR TREATMENT

INTERFERONS ARE BY AND LARGE PART OF THE PAST AND NOT RECOMMENDED ANYMORE

Approved DAAs From Multiple Classes: Basis of 2019 Combination HCV Regimens



NOMENCLATURE

- EVIR
  - NS3/4 targeting protease inhibitors
    - Simeprevir
    - Paritaprevir
    - Grazoprevir
    - Glecaprevir
    - Non-nucleotide: Dasabuvir
- UVIR
  - NS5B targeting polymerase inhibitors
    - Nucleotide: Sofosbuvir
    - Non-nucleotide: Dasabuvir

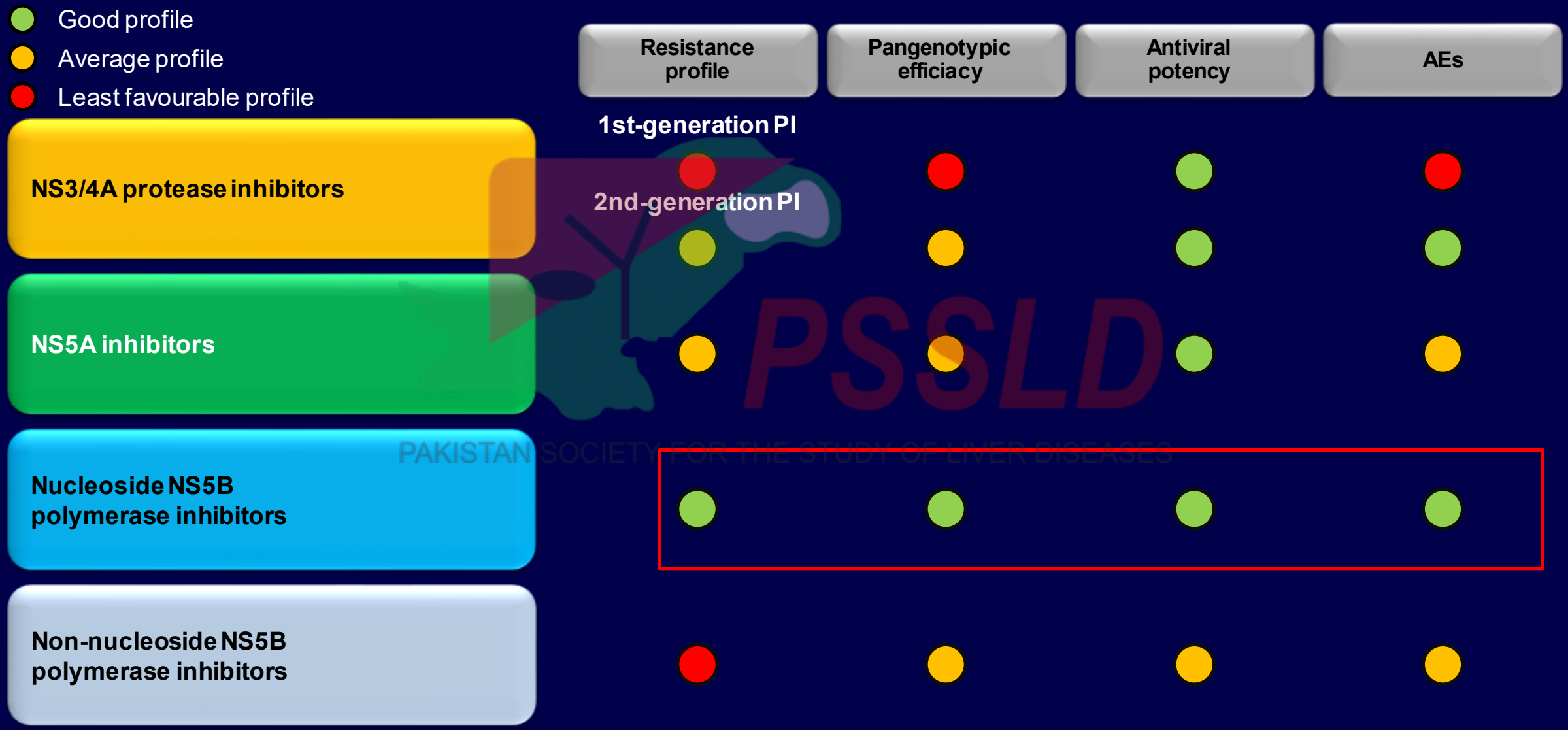
- AVIR
  - NS5A targeting agents
    - Ledipasvir
    - Ombitasvir
    - Elbasvir
    - Velpatasvir
    - Pibrentasvir

REMEMBER

- Protease inhibitors can be bad as they have multiple drug interactions and may cause decompensation in patients with significant fibrosis.

- Ribavirin can be bad in people with hemolytic tendency and may cause severe hemolysis

DAAs: the building blocks for new HCV treatment regimens



PI = protease inhibitor.

Adapted from Lange C, et al. EMBO Mol Med 2014; 6: 4–15

DAAs: the building blocks for HCV treatment regimens

NS3/4A protease inhibitors	• Grazoprevir • Paritaprevir • Simeprevir	• Glecaprevir • Voxilaprevir
NS5A inhibitors	Daclatasvir Ledipasvir Elbasvir Valpatsavir	Pibrentasvir Ruzasvir
Nucleoside NS5B polymerase inhibitors	• Sofosbuvir	
Non-nucleoside NS5B polymerase inhibitors	• ABT-333 (dasabuvir)[1] • BMS-791325 (beclabuvir)[1]	• Uprifosbuvir (formerly MK-3682)

DAA'S APPROVED IN 2014

DAA'S APPROVED IN 2015

DAA'S APPROVED IN 2016

DAA'S APPROVED IN 2019

Investigational DAA'S

AASLD 2019 GUIDELINES FOR HCV NAÏVE PATIENTS TREATMENT

AASLD/IDSA Recommendations: Initial Therapy for Genotype 1 HCV Infection

HCV GT	No Cirrhosis	Compensated Cirrhosis
1	EBR/GZR 12 wks* GLE/PIB 8 wks LDV/SOF 8-12 wks† SOF/VEL 12 wks	EBR/GZR 12 wks* GLE/PIB 12 wks LDV/SOF 12 wks SOF/VEL 12 wks

*Only if no baseline NS5A RAS for GT 1a; if NS5A RAS present for GT 1a, EBR/GZR not recommended.
†8 wks of LDV/SOF only if non-black race, HIV-uninfected, and HCV RNA < 6 million IU/mL.

AASLD/IDSA. HCV guidance. 2019.

AASLD/IDSA Recommendations: Initial Therapy for Genotype 2 or 3 HCV Infection

HCV GT	No Cirrhosis	Compensated Cirrhosis
2/3	GLE/PIB 8 wks SOF/VEL 12 wks	GLE/PIB 12 wks SOF/VEL 12 wks* SOF/VEL/RBV 12 wks SOF/VEL/VOX 12 WKS

*Only if no baseline Y93H for GT 3. If Y93H present for GT3, add RBV or choose alternative regimen (consider SOF/VEL//VOX).

AASLD/IDSA. HCV guidance. 2019.

AASLD/IDSA Recommendations: Initial Therapy for Genotype 4 HCV Infection

HCV GT	No Cirrhosis	Compensated Cirrhosis
4	EBR/GZR 12 wks GLE/PIB 8 wks LDV/SOF 12 wks SOF/VEL 12 wks	EBR/GZR 12 wks GLE/PIB 12 wks LDV/SOF 12 wks SOF/VEL 12 wks

AASLD/IDSA. HCV guidance. 2019.

AASLD/IDSA Recommendations: Initial Therapy for Genotype 5 or 6 HCV Infection

HCV GT	No Cirrhosis	Compensated Cirrhosis
5/6	GLE/PIB 8 wks LDV/SOF 12 wks SOF/VEL 12 wks	GLE/PIB 12 wks LDV/SOF 12 wks SOF/VEL 12 wks

AASLD/IDSA. HCV guidance. 2019.

First-line HCV Therapy: Distinguishing Among Recommended Options

EBR/GZR - QD single tablet
12 wks, GT 1 or 4
Requires RAS testing for GT1a
Contains PI: ***do not use*** if decompensated
Can be used in stage 4/5 CKD
DDI highlights: glucocorticoids, statins, PDE inhibitors, rifampin

GLE/PIB - QD 3 tablets with food
8 wks no cirrhosis, 12 wks if cirrhosis, GT 1-6
No RAS testing
Contains PI: ***do not use*** if decompensated
Can be used in stage 4/5 CKD
DDI highlights: statins, rifampin

LDV/SOF - QD single tablet
8-12 wks, GT 1, 4, 5, or 6
No RAS testing
Safe in decompensation
Not recommended for stage 4/5 CKD
DDI highlights: acid-reducing agents, statins, rifampin

SOF/VEL - QD single tablet
12 wks, GT 1-6
Requires RAS testing for some GT 3
Safe in decompensation
Not recommended for stage 4/5 CKD
DDI highlights: acid-reducing agents, rifampin

AASLD/IDSA. HCV guidance. 2019.

Factors to be considered in HCV therapy in Naïve Patients

- IFN Exposed
- IFN Naïve

- Renal Failure
- Co Morbids
- Co Infections
- Transplantation

Available DAA in Pakistan

- Sofosbuvir
- Ledipasvir
- Daclatasvir
- Velpatasvir
- Voxilaprevir

Ribavirin as add on in selective patients

DAA exposed: non responders/relapsers

- HCV RNA sequencing and allele identification

  – Dr Ghazala Rubi: Incharge PCR Section: PGMI/LGH, PINS Building

  – DR Bilal Nasir: Assistant Professor of Gastroenterology, PGMI/LGH

Pls help by contributing blood samples

THANK YOU !!!!

PSSLD

PAKISTAN SOCIETY FOR THE STUDY OF LIVER DISEASES