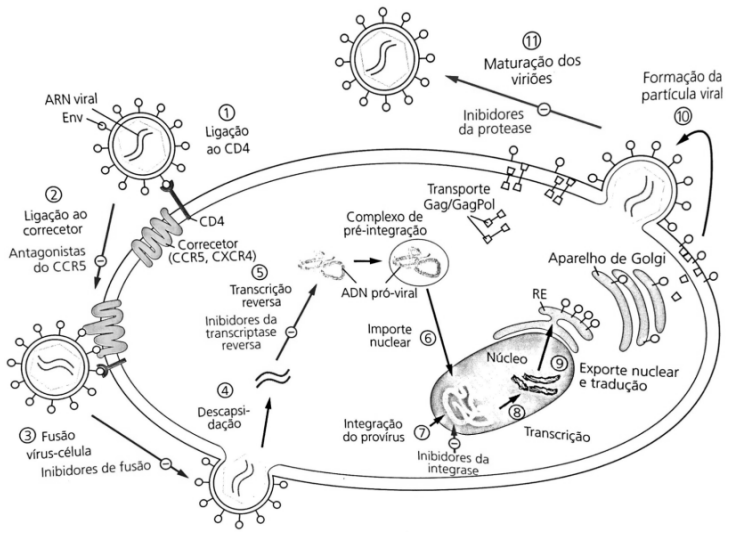
ANTIVIRAIS

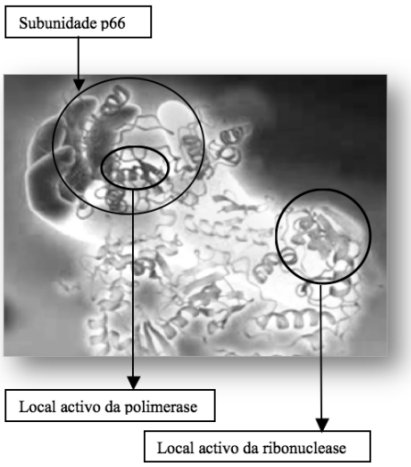
AulaTP

Antirretrovirais

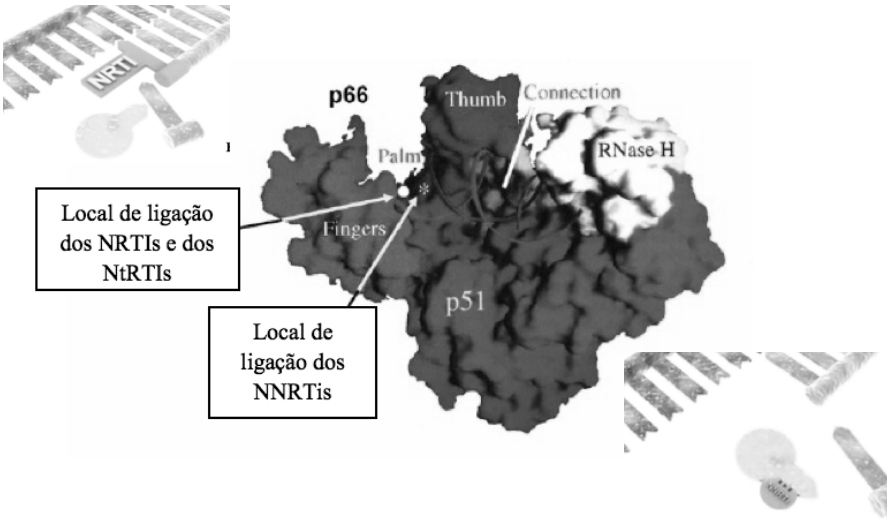
Ciclo de replicação HIV



Transcriptase reversa

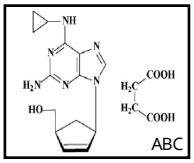


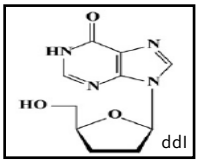
Transcriptase reversa

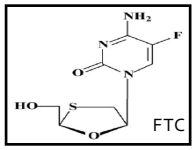


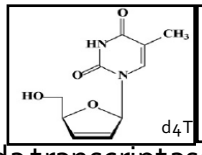
Inibidores análogos dos nucleosídicos/nucleotídicos da TR

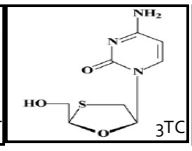
- Inibidores nucleosídicos da transcriptase reversa
  - Abacavir
  - Didanosina
  - Emtricitabina
  - Estavudina
  - Lamivudina
  - Zidovudina

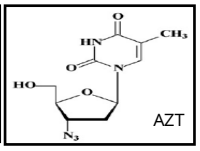




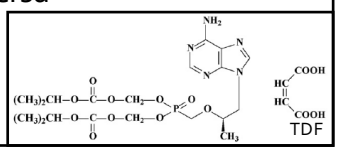




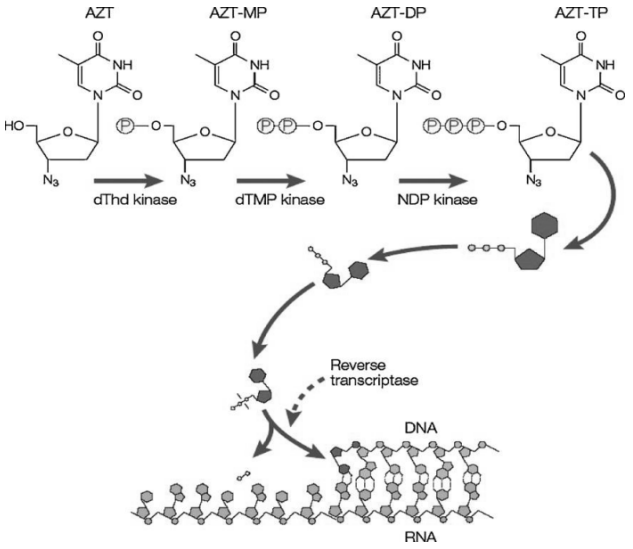




- Inibidor nucleotídico da transcriptase reversa
  - Tenofovir

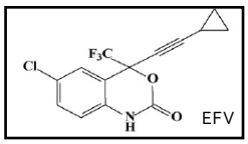


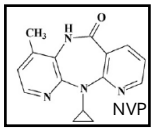
Mecanismo de ação da zidovudina

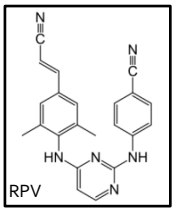


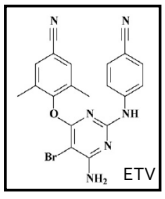
Inibidores não nucleosídicos da TR

- Inibidores não-nucleosídicos da transcriptase reversa
  - 1ª geração
    - Nevirapina
    - Efavirenz
  - 2ª geração
    - Rilpivirina
    - Etravirina

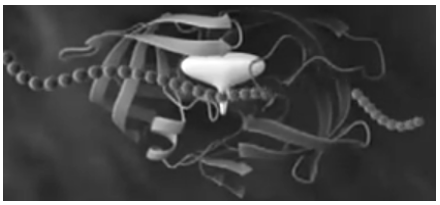


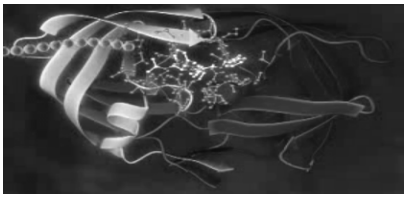






Inibidores da Protease

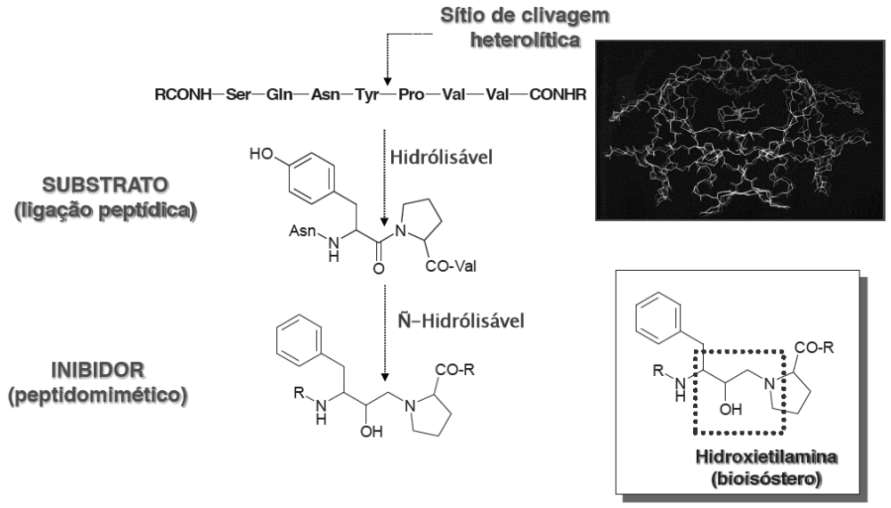




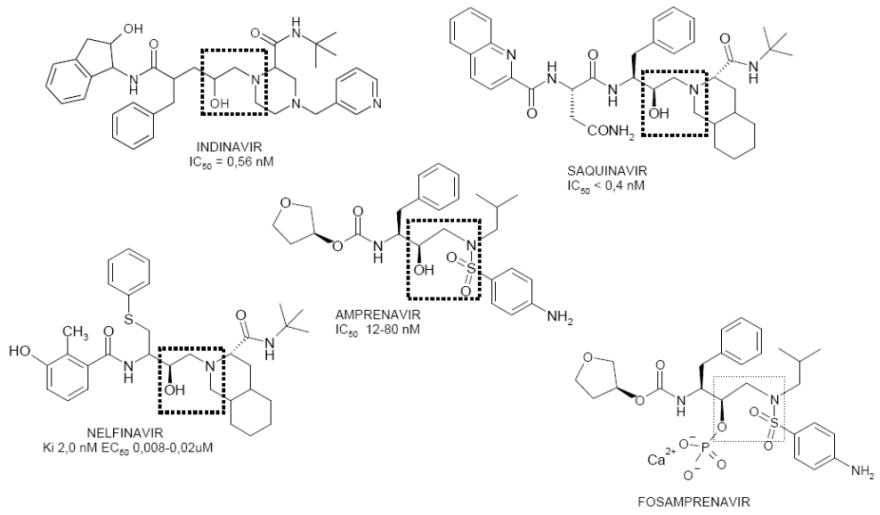
Inibidores da Protease

- Inibidores da protease
  - Atazanavir
  - Darunavir
  - Fosamprenavir
  - Indinavir
  - Nelfinavir
  - Lopinavir
  - Saquinavir
  - Amprenavir
  - Tipranavir
    - Ritonavir

Inibidores da Protease

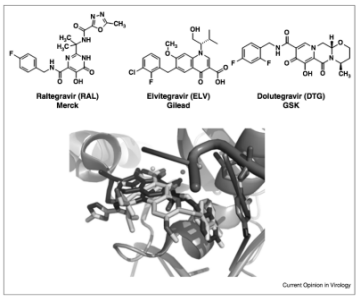


Inibidores da Protease



Inibidores da integrase

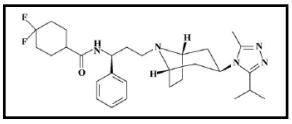
- Inibidores da integrase
  - Raltegravir (aprovado 10/07)
  - Elvitegravir* (aprovado 8/12)
  - Dolutegravir (aprovado 8/13)



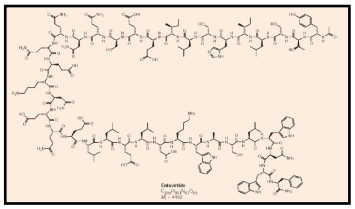
Chemical structures of RAL, EVG, and DTG and overlay in the integrase active site. All three InSTIs engage the critical Mg ions (green balls) and stack with 3' end of the viral DNA (shown in blue) in the complex.

Inibidores da entrada

- Inibidores do coreceptor CCR5
  - Maraviroc



- Inibidores da fusão
  - Efuvirtide



ART / TARc – Recomendações Portuguesas

- Terapêutica Antirretroviral Combinada

Tabela 3: Início da terapêutica antirretrovírica combinada (TARc) em doentes adultos e adolescentes com infeção crónica por VIH-1: regimes preferenciais.

A	B	Observações
NNITR	**N(t)ITR**	
EFV	**TDF/FTC** ou **ABC/3TC**	TDF/FTC coformulado em comprimido único. ABC/3TC coformulado em comprimido único. EFV/TDF/FTC coformulado em comprimido único.
NVP	**TDF/FTC**	TDF/FTC coformulado em comprimido único.
IP potenciado com Ritonavir	**TDF/FTC** ou **ABC/3TC**	
ATV/r		ATV/r: 300/100 mg *qd*.
DRV/r		DRV/r: 800/100 mg *qd*.
ITI		
RAL	**TDF/FTC**	

2012

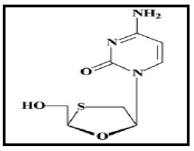
Hepatite B

Hepatite B

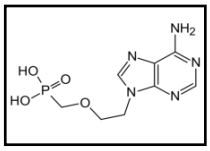
- Análogos dos Nucleótidos/nucleósidos
  - Lamivudina (análogo dos nucleósidos)
  - Adefovir (análogo dos nucleótidos)
  - Entecavir (análogo dos nucleósidos)
  - Telbivudina (análogo dos nucleósidos)

Hepatite B

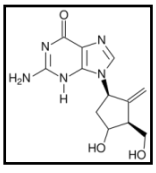
Lamivudina



Adefovir



Entecavir



Interferões-alfa disponíveis para o tratamento da hepatite B.

INF-α-2b	Intron A®
IFN-α-2ª	Pegasys®

Hepatite C

Hepatite C

Fármacos utilizados na terapêutica do vírus da hepatite C.

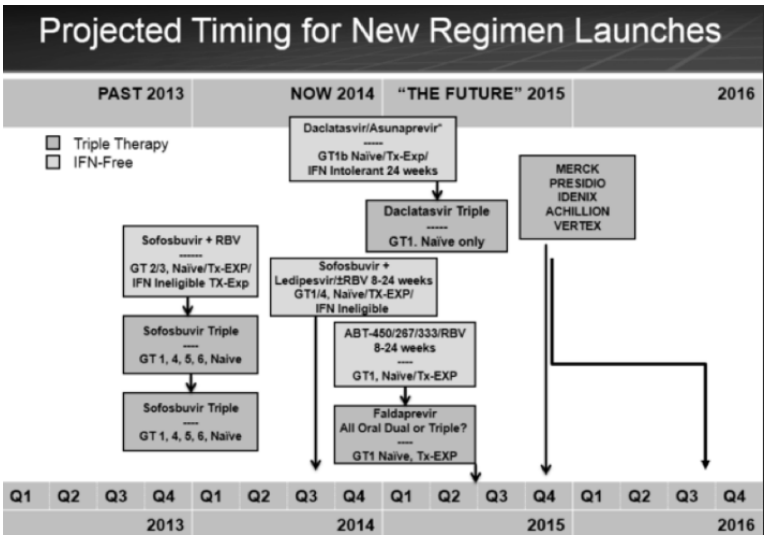
Terapia imunomodelatória	Interferão-alfa-2[a]
	Interferão-alfa-2b
	Interferão-alfa-2a peguilado
	Interferão-alfa-2b peguilado
Terapia antiviral	Ribavirina

Interferão-alfa-2a;
Interferão-alfa-2b;
Interferão-alfacon-1[8o]
interferão-n1.[8o]

Hepatite C

- Interferão peguilado (PEG-INF) + Ribavirina
- Inibidores da protease NS3
  - Telaprevir
  - Boceprevir

Pipeline



DAAs

Many Direct Acting Antivirals in Development

- **Protease inhibitors**
  - Faldaprevir
  - Asunaprevir
  - ABT-450
  - MK-5172
  - Sovaprevir
  - ACH-2684
  - GS-9451 NAIAD Synergy trial
- **NS5A Inhibitors**
  - Daclatasvir
  - Ledipasvir
  - ABT-267
  - GS-5816 pangenotypic
  - ACH-3102
  - PPI-668
  - GSK 2336805
  - Samatasvir
  - MK-8742

DAAs

Direct-Acting Antiviral Agents (DAAs) - Key Characteristics

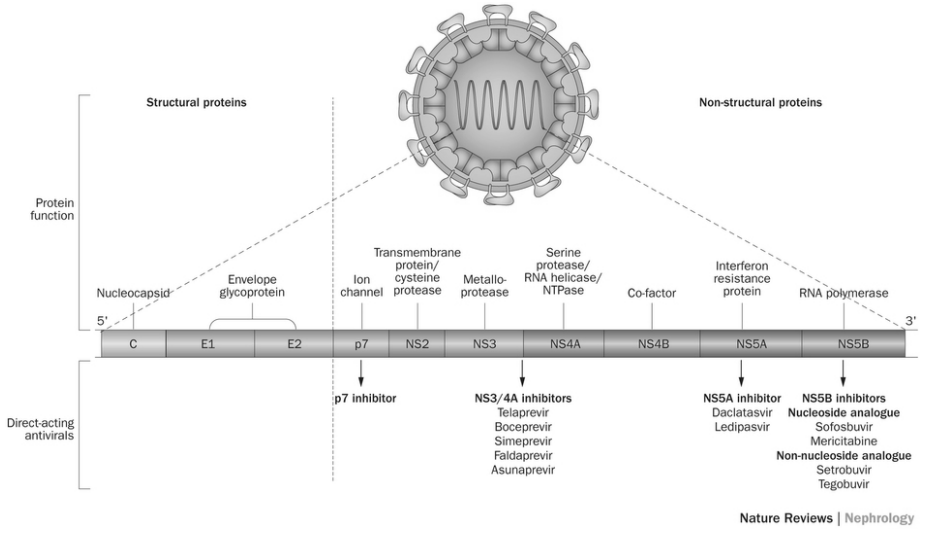
NS3 /4A Inhibitors (Protease inhibitor PI)
High potency
Limited genotypic coverage
Low barrier to resistance

NS5B Nucleos(t)ide Inhibitors (NI)
Intermediate potency
Pan genotypic coverage
High barrier to resistance

NS5A Inhibitors
High potency
Multi-genotypic coverage
Low barrier to resistance

NS5B Non Nucleoside Inhibitors (NNI)
Intermediate potency
Limited genotypic coverage
Low barrier to resistance

HCV - DAAs



Guidelines

CrossMark

EASL | JOURNAL OF HEPATOLOGY

EASL Recommendations on Treatment of Hepatitis C 2015

European Association for the Study of the Liver*

Table 5. Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients and patients who failed on a treatment based on PegIFN-α and ribavirin (RBV).

Patients	PegIFN-α, RBV and sofosbuvir	PegIFN-α, RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 1a	12 wk	12 wk, then PegIFN-α and RBV 12 wk (treatment-naïve or relapsers) or 36 wk (partial or null responders)	No	8-12 wk, without RBV	12 wk with RBV	No	12 wk without RBV	12 wk without RBV
Genotype 1b					12 wk without RBV			
Genotype 2	12 wk	No	12 wk	No	No	No	No	12 wk without RBV
Genotype 3	12 wk	No	24 wk	No	No	No	No	12 wk without RBV
Genotype 4	12 wk	12 wk, then PegIFN-α and RBV 12 wk (treatment-naïve or relapsers) or 36 wk (partial or null responders)	No	12 wk without RBV	No	12 wk with RBV	12 wk without RBV	12 wk without RBV
Genotype 5 or 6	12 wk	No	No	12 wk without RBV	No	No	No	12 weeks without RBV

Table 6. Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients and patients who failed on a treatment based on PegIFN-α and ribavirin (RBV).

Patients	PegIFN-α, RBV and sofosbuvir	PegIFN-α, RBV and simeprevir	Sofosbuvir and RBV	Sofosbuvir and ledipasvir	Ritonavir-boosted paritaprevir, ombitasvir and dasabuvir	Ritonavir-boosted paritaprevir, and ombitasvir	Sofosbuvir and simeprevir	Sofosbuvir and daclatasvir
Genotype 1a	12 wk	12 wk (treatment-naïve or relapsers) or 24 wk (partial or null responders)	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	24 wk with RBV	No	12 wk with RBV, or 24 wk without RBV	12 wk with RBV, or 24 wk without RBV
Genotype 1b					12 wk with RBV			
Genotype 2	12 wk	No	16-20 wk	No	No	No	No	12 wk without RBV
Genotype 3	12 wk	No	No	No	No	No	No	24 wk with RBV
Genotype 4	12 wk	12 wk (treatment-naïve or relapsers) or 24 wk (partial or null responders)	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	No	24 wk with RBV	12 wk with RBV, or 24 wk without RBV	12 wk with RBV, or 24 wk without RBV
Genotype 5 or 6	12 wk	No	No	12 wk with RBV, or 24 wk without RBV, or 24 wk with RBV if negative predictors of response	No	No	No	12 wk with RBV, or 24 wk without RBV

FIM