WHAT'S NEW IN THERAPEUTICS?

MEDICAL UPDATE GROUP

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Sadeck Vawda

What's new in Therapeutics?

1. CAR T CELL THERAPY
2. 3D Printing: the Future of manufacturing medicines?
3. Photo pharmacology: using light to activate drugs
4. Hepatitis C: Latest advances in therapy
5. PrEP – HIV prevention strategy
6. Miscellaneous

I. CAR T CELL THERAPY

- Engineering patients' immune cells to treat their cancers

CAR T CELL THERAPY

- For years, foundations of cancer treatments were Surgery, Chemotherapy and Radiation Therapy.
- Over the last 2 decades, targeted therapies have cemented themselves as standard treatments for many cancers e.g. Imatinib, Transtuzumab.
- Over the past years, Immunotherapy to enlist and strengthen a patient immune system has emerged as the "Fifth Pillar" of Cancer Treatment.
- A rapidly emerging immunotherapy is CAR T Therapy.

CAR T CELL THERAPY

- Has captured the attention of researchers in small clinical trials, in patients with advanced blood cancers.
- Remarkable responses in some patients from whom all other treatments were ineffective.

CAR T CELL THERAPY

In 2017, Two Car T Therapies were approved by USFDA

- One for the treatment of children with acute lymphoblastic leukemia (ALL)
- One for the treatment of adults with advanced lymphomas.

CAR T CELL THERAPY

- Equivalent of giving patients a living drug
- Back bone of CAR T Cells is T Cells (Workhorses of the immune system. Critical role in orchestrating the immune response and killing cells infected by pathogens).

CAR T CELL THERAPY

- Therapy consists of drawing blood from patients and separating out the T cells.
- Next using a disarmed virus, the T cells are genetically engineered to produce receptors on their surface called Chimeric Antigen Receptors or CARs.
- These receptors are synthetic molecules that allow the T cells to recognize and attached to a specific protein, antigen or tumor cells
- Once the collected T cells have been engineered to express the antigen-specific CAR, they are "expanded" in the laboratory into hundreds of millions.
- The final step is the infusion of the CAR T Cells into the patients.

CAR T CELL THERAPY

- The Engineered cells further multiply in the patient's body and with guidance from their engineered receptors, recognize and kill cancer cells.
- Advances in intracellular engineering of CAR T cells have improved T cell's ability to replicate after infusion and survive longer in circulation.
- To produce a Batch of CAR T cells in the laboratory takes less than 7 days.

CAR T CELL THERAPY

- Initial development of CAR T cells therapies has focused largely on ALL, the most common cancer in children.
- More than 80% of children with ALL that arises in B cells - the predominant type of pediatric ALL – will be cured by intensive chemotherapy.
- For those who relapse after chemotherapy or stem cell transplant, treatment options are close to none.
- ALL is a leading cause of death from childhood cancer.
- In the initial trials in children with ALL not responding to existing therapies or has recurred, CAR T Cells therapy provided a complete response in 27 out of 30 patients with many patients showing no signs of recurrence long after treatment.
- Single treatment

CAR T-Cell Therapy

- These early successes laid the foundation of a CD-19 targeted Car T-Cells therapy called Tisangenlecleucel (Kymriah) for children and adolescents with ALL
- Many of the patients had complete and long lasting remissions
- Based on the trial results, FDA approved the drug in August 2017
- There are no shortage of promising data on CAR T-cells to treat adult patients with blood cancers
- Findings from a large trial has led to the approval of a second CAR T-Cell product (Axicabtagene Ciloleucel (Yescarta) in some patients with Lymphoma).

CAR T-Cell Therapy

- Results to date in Lymphomas have been incredibly successful
- CAR T-Cell are almost certain to become a frequently used therapy for several types of Lymphomas.
- Rapid advances in and growth of Car T-Cell Therapy has exceeded all expectations

CAR T-Cell Therapy

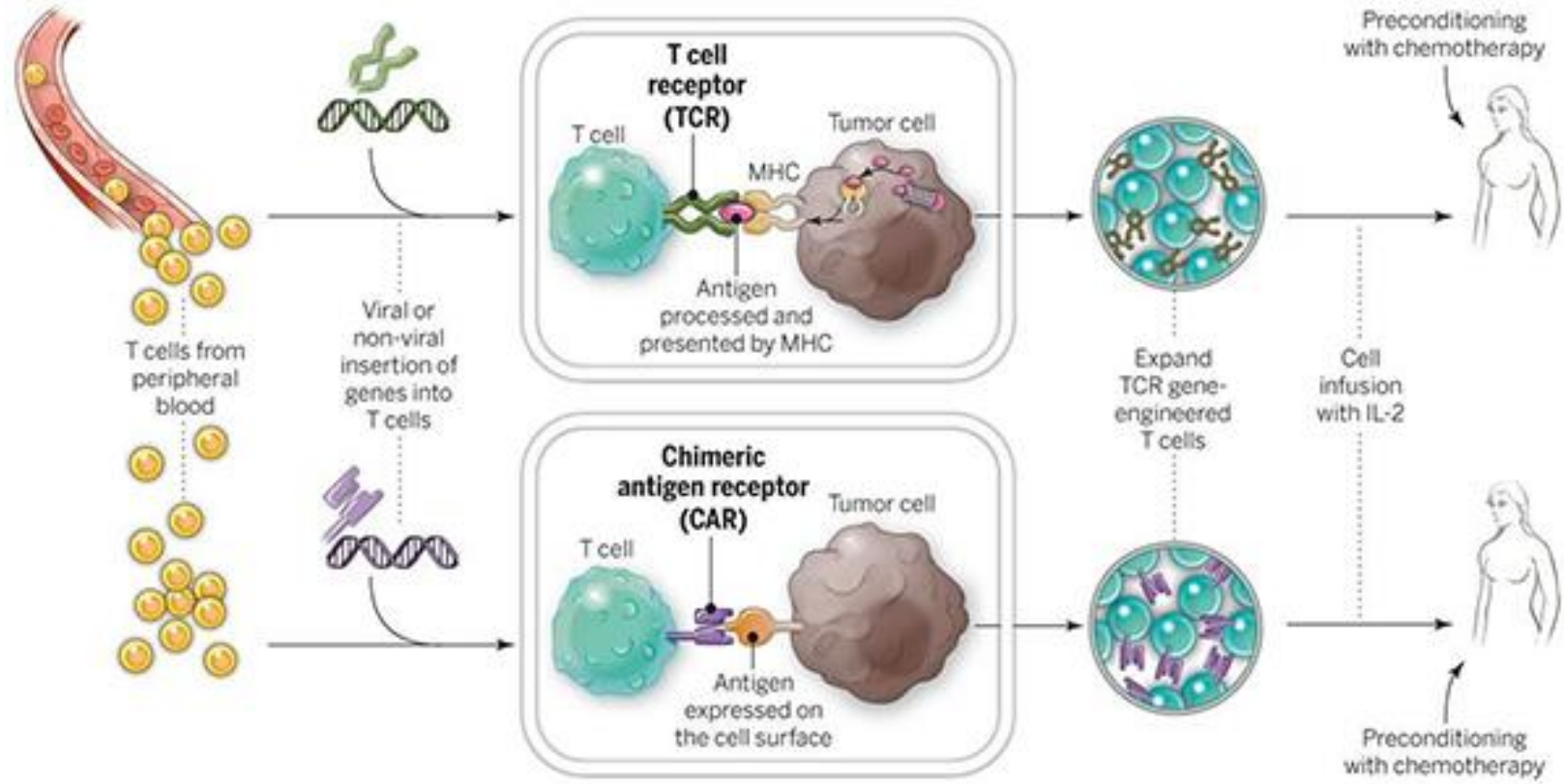
Understanding/Managing Side Effects

- Like all cancer therapies, CAR T-Cell therapy can cause several worrisome and sometimes fatal side effects.
- One of the most frequent is Cytokine Release Syndrome (CRS).
- Cytokines are released by T Cells as part of their immune duties to stimulate and direct the immune system.
- In CRS, there is a massive release of cytokines in the blood stream which can lead to dangerously high fever and precipitous drops in blood pressure.

CAR T-Cell Therapy

Understanding/Managing Side Effects

- CRS is managed with standard supportive therapies including steroids
- Research has shown that patients with severe CRS had particularly high levels of IL-6, a cytokine secreted by T-Cells.
- Tocilizumab (Actemra) which blocks IL-6 activity resolves the problem in most patients and has become a standard therapy for severe CRS.
- Another side effect of CAR T-Cell therapy is a mass die off of B cells (B cells aplasia). B cells are killed by CAR T-Cells. To compensate, many patients are given immunoglobulin therapy in order to have the necessary antibodies to fight infection.
- Another potentially fatal side effect is cerebral edema.


T cells from peripheral blood
Viral or non-viral insertion of genes into T cells
T cell receptor (TCR)
T cell
Tumor cell
MHC
Antigen processed and presented by MHC
Chimeric antigen receptor (CAR)
T cell
Tumor cell
Antigen expressed on the cell surface
Expand TCR gene-engineered T cells
Cell infusion with IL-2
Preconditioning with chemotherapy
Preconditioning with chemotherapy

CAR T-Cell Therapy

The Future

- Research is continuing at a swift pace. Mostly in patients with blood cancers
- The number of trials has expanded exponentially (>180)
- Antigen targets for Car-T Cell therapy have been identified in other blood cancers including multiple myeloma.

CAR T-Cell Therapy

The Future

- Research ongoing for solid tumors as well though there is some skepticism whether it will have the same success.
- Finding suitable antigens to target on solid tumors is a challenge
- Majority of tumor antigen in solid tumors reside inside tumor cells out of reach of CAR, which can only target surface antigens.
- Another line of research is to use cells not collected from the patient but from healthy donors – "off the shelf approach"
- The future looks bright for CAR T-Cell therapy.

2.

3D Printing – the future of manufacturing medicines?

3D Printing

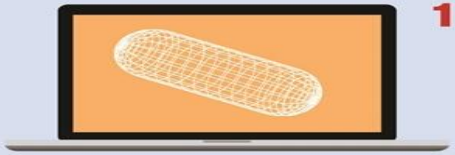
- Promises a future of drugs printed on demand, to custom doses and the possibility that cost may no longer be a barrier to making niche medicines.

- Children could be among the patients to benefit most.

A 3D printer works by adding layer by layer until a 3D shape emerges

How does a 3D printer work?

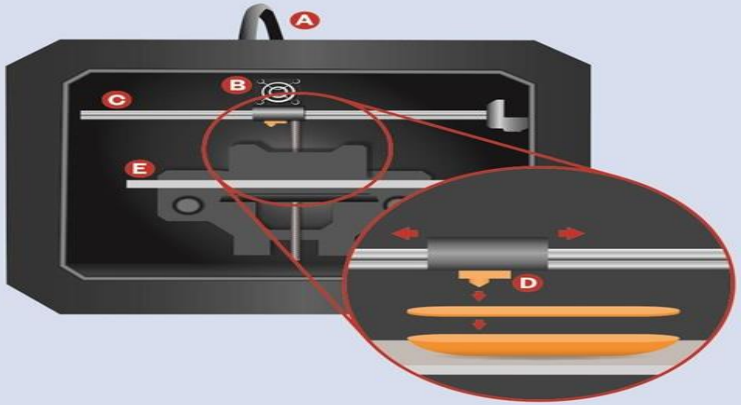
3D printing involves making solid objects from a digital file by printing thinly-sliced, horizontal layers in any shape. 3D printing technology was developed in the 1980s, but the first "off-the-shelf" 3D printer did not become publicly available until 2009.



1 An original idea is designed using a digital modelling programme such as CAD (computer-aided design) or animation modelling software.

2 Once the design is completed, the file is sent to the 3D printer. The 3D printer makes passes (like an inkjet printer) over the build plate, depositing layer upon layer of material to create the finished product.

- **A Filament guide tube** The material, in this case a blend of polymer and drug, is fed through the tube
- **B Extruder** Melts the drug polymer blend
- **C Gantry** Allows the extruder to move from side to side and front to back
- **D Extrusion nozzle** Molten filament is fed through the nozzle
- **E Build plate** Moves down once each layer is finished, thus helping the nozzle build additional layers



3 The different layers are fused throughout the process to create a single 3D object.

Changing the shape of the tablet affects the speed at which the drug is released in the body

Sectioned plain tablet

Sectioned bilayer tablet

Sectioned multilayer tablet

Sources: Makerbot, Mashable.com, On3dprinting.com, GR; Alvaro Goyanes

3D Printing

The potential of 3D printing is about being able to deliver what you want when you want.

3D Printing

- The technology could revolutionize the way we look at children's medicine both in terms of what they take and ability to keep changing the dose as they grow.
- Having a 3D printer in a hospital personalized pharmacy could make weekly medications change simple and even fun.
- Real world applications are some years off, perhaps around 10 years.

3D Printing

- Democratizing pharmaceuticals.
- 3D printing will allow personalization and will improve distribution especially in the developing world.
- Increase access to medicine.

3D Printing

- To get printing off the ground first requires interest from industrial partners.
- Lots of research ongoing on applications of 3D to drug manufacture.
- The key drivers for using 3D printing as a method of manufacture are the ability to be more precise and to make drugs more patient friendly. It can ultimately improve adherence by alleviating medication avoidance due to hard to swallow or hard to administer dosage forms.

3D Printing

Challenges

- Optimization and improvement of software performance.
- Development of excipients for application in 3D formulations
- Manufacturing drug using 3D printing will need to comply with regulations.
- It will need to be manufactured under the supervision of someone with a license to operate a 3D printer to dispense drugs to avoid medication errors or illegal printing of drug products.
- Uniformity of the drug/dosage form will need to be validated.
- Quality control aspects.
- Clinical studies to assess safety, efficacy and stability of new 3D based formulations.

3D Printing

- USFDA recently approved the first 3D printed drug product.
- Indicative of a new chapter in pharmaceutical manufacturing.
- “Spritam” tablet, the first 3D printed drug approved, contains levetiracetam for epilepsy. This innovative product disintegrates in the mouth with the sip of a liquid and offers a new option to patients, including those who struggle to take their medicines.

3D Printing

- Will 3D printer replace drug manufacturing as we know it?
- Is it more likely that 3D printing's future lie alongside traditional ways of making pills?
- The technology will be used probably for niche products that might not be manufactured otherwise.
- 3D printing as a platform technology will have competitive advantages for complex products, personalized products and products made on demand.
- 3D printing will allow the preparation of dosage forms with multiple active ingredients, will offer the desired precision and accuracy especially for potent drugs that are applied in small doses and will cause a reduction in material wastage.

3D Printing

- These advantages create opportunities to improve the safety, efficacy and accessibility of medicines.
- 3D technology opens the door to a new era of advanced drug delivery with built in flexibility suited for personalized/customied medicines.
- It is expected that 3D printing will revolutionize the development of new generations of pharmaceutical formulations.

3.

Photopharmacology: using light to activate drugs

- Most of the drugs available on the market rely on the use of bio-active compounds.
- Pharmacological response is elicited by interactions with molecular targets including receptors, enzymes, ion channels, etc.

Selectivity

Selectivity is essential and the lack these of causes side effects and also limits increased dose at the site of action.

Selectivity can be achieved through several avenues:

1. In antimicrobials, by selecting targets specific to microbes and not to humans.
2. By selection of targets in specific organs and over expressed only in selected diseases as in cancer chemotherapy.
3. Local administration of a drug, e.g. in ophthalmology.

In general, it is difficult to achieve selectivity as the potential targets are expressed throughout the body in both diseased and healthy tissues.

- One potential approach that scientists are looking at in order to solve the issues of selectivity is by designing drugs whose activity can be regulated with light
  - → Science of photopharmacology

- Selectivity can hence be achieved with a reduction of systemic side effects.

- The concept of photopharmacology relies on the use of light to activate drugs when and where needed.

Photopharmacology

- Photo-activation can be achieved either outside the body or inside the body or at the site of action.
- The drugs used in photo pharmacology contain light switching molecules that could be used for targeted therapies with minimal side effects.
- These photo switches are entities that modify their structure upon light irradiation

Photopharmacology

Research is being undertaken to use these therapies to tackle blindness, cancer, diabetes and antibiotic resistance.

- Light is already being used in medicine. For e.g.

a) Photodynamic therapy in age-related macular degeneration.
b) Use of photo activated molecules, e.g. psoralens in psoriasis.

Photopharmacology

- Photopharmacology is presently at the stage of defining molecular targets.
- The photo switch needs to be a molecule that has two isomers, which could be switched on using light. The isomers need to have vastly different shapes, so the switch is likely to also alter the conformation of any attached drug hence the drug's ability to reach its biological target.
- This way light could be used to switch drug activity on and off.
- One molecule being used in research as a photo switch is azobenzene.

Photopharmacology

- The idea of using photoswitchable drugs has created a lot of interest and research.
- It remains to be seen whether photopharmacology is clinically practical.
- Main issue is the ease and safety of penetrating the body with light. UV light can damage cells.
- Too early to assess the prospects of photopharmacology in clinical practice. The hunt goes on for new photo switches and technology.

4. HEPATITIS C: LATEST ADVANCES IN THERAPY

HEPATITIS C

- Global health problem with an estimated 185 million people infected worldwide
- 3 to 4 millions new infections every year
- In 2000, research work by Alter and Houghton led to the discovery of the hepatitis C virus and a screening test to prevent transmission of the infection through blood transfusion.
- 6 major genotypes of the virus, known as hepatitis C genotypes 1 to 6
- Recent years have seen an evolution in the treatment of hepatitis C infection with new antivirals emerging at remarkable speed that promise cure rates never thought previously possible
- There are no vaccines for hepatitis C at the moment

HEPATITIS C

GENOTYPES

- 1 to 6

- Genotype 1 is more prevalent comprising more than 46% of all cases.

- Genotype 3 comprises 30% of all cases, while genotypes 2,4 and 6 account for around 23% of all cases. Genotype 5 accounts for the remaining 1%.
- Egypt: highest prevalence(15%), type 4 prevalent, major health epidemic

HEPATITIS C

Mauritius

- Prevalence: around 1% of the population (around 12,000 infected persons)
- It is estimated that 95% of those infected are PWID
  - Genotype 1 and 2 most common (based on reports by NGOs)
  - Screening test available
  - Genotyping facilities, viral load measurement are not available

HEPATITIS C

TRANSMISSION

There are several routes for Hepatitis C virus transmission:

1. People who inject drugs (PWID) are at risk due to sharing unsterilized injecting paraphernalia. Around 50% of PWID in the UK are chronically infected with Hepatitis C virus.

2. Vertical transmission from mother to child occurs in around 2% of mothers with Hepatitis C. Can be as high as 20% in mothers coinfected with HIV.

HEPATITIS C

Transmission

3. Sexual exposure is a rare cause of transmission and is estimated to account for less than 1% of cases. Risk increases in those who engage in sexual practices in which risk of blood contact is increased.
4. Transfusion is now a rare cause of transmission following improved donor screening and viral inactivation of plasma products. Before these developments, patients who received infected blood products (e.g. haemophiliacs) were at the highest risk.
5. Occupational exposure is a possible risk e.g (needle stick injuries) which can be minimised by safe working practices.
6. Other possible causes include tattooing, acupuncture, dental work and piercing. These risks can be minimized if good infection control practices are followed.

HEPATITIS C

Prognosis

- Hepatitis C is termed a silent killer
- It causes slow but progressive liver damage
- After initial infection with the Hepatitis C virus, around 75-85% of patients will fail to clear the virus and will become chronically infected
- These patients will often be assymptomatic until they present with signs of end-stage liver diseases. (e.g. Ascites, Hepatic Encephalopathy, etc)

HEPATITIS C

Prognosis

- The remaining 15-25 % go on to clear the infection and develop antibodies. It is important that patients are informed that spontaneous clearance of Hepatitis C does not mean they are immune, and re-infection can occur.

- It is estimated that around 30% of chronically infected patients will develop cirrhosis within 20 years and 5% will develop Hepatocellular Carcinoma.

- Risk factors for accelerated progression include male gender, older age, obesity, infection with HIV, diabetes and a significant alcohol history.

HEPATITIS C

Laboratory diagnosis

- Anti Hepatitis C antibodies are usually present three to six months after infection. Diagnosis is made through a Hepatitis C antibody test and a confirmatory CRNA test to assess for active infection(PCR)

- Oral fluid testing is possible but is of lower sensitivity and specificity.

HEPATITIS C

Life cycle

- HCV is a blood borne single stranded RNA virus.
- RNA viruses mutate to a greater extent than DNA viruses, resulting in difficulty for the body's immune system to locate and destroy them

- Steps in the life cycle
  - Entry in the host cell (Hepatocyte)
  - Uncoating of the viral genome
  - Translation of viral proteins
  - Viral genome replication
  - Assembly and release

TARGETS FOR NEW DRUGS

- Non structural proteins are essential for the viral life cycle processes and are the primary tagets for the new antiviral medicines.

- In particular the viral enzyme NS3/4 protease (important in viral protein production) and non structural proteins NS5A and NS5B (which play a role in HCV replication) are targets.

TREATMENT

- The primary aim of the treatment is to achieve viral eradication or sustained viral response (SVR)
- SVR is the most widely used end point for hepatitis C treatment. It is a durable marker of viral eradication.
- Traditional time point to assess if SVR achieved is at 24 weeks post treatment though 12 weeks post treatment is now widely recognised.
- Secondary aims:
  - Preventing transmission
  - Preventing progression of liver damage
  - Improving patients quality of life

TREATMENT

- Response rates to treatment are dictated by genotype, treatment history and patient specifics (age, gender, other infections present, etc)

- The stage of liver disease is also an important predictor of viral response. Those with advanced fibrosis or cirrhosis achieve lower treatment response rates

CURRENT TREATMENT

Peginterferon and ribavirin

Peginterferon

- Peginterferon and ribavirin combination therapy is an established treatment for Hepatitis C infection
- Peginterferon available as Alfa 2A and Alpha 2B. They are administered by subcutaneous injection once weekly.
- Dose may be adjusted depending on clinical factors such as presence of thrombocytopenia and low mood.

Ribavirin

- Oral tablet administered twice daily with food. Dose of ribavirin is often adjusted to account for the presence or absence of anaemia.

CURRENT TREATMENT

Peginterferon and ribavirin

- Treatment duration ranges from 24 to 72 weeks with SVR 24 rates of around 40-50% in patients with Hepatitis C genotype 1 and 40-80% in patients with genotypes 2 to 6.

- The peginterferon/ribavirin regimen has an extensive side effect profile including cytopenia and mood disturbances.

CURRENT TREATMENT

Peginterferon and ribavirin

- These limit its use in some patients and it is estimated that around 27% of patients prescribed a peginterferon stop treatment due to adverse effects.

- Side effects of ribavirin include dermatological side effects (dermatitis, pruritus, urticaria, etc) and haemotological abnormalities (e.g anaemia)

New drugs for Hepatitis C

- A new era has started in 2015 with the new DAA (directly acting antivirals) in the management of hepatitis C.
- These new drugs have revolutionized the treatment of hepatitis C.
- They represent a major advance in the management of hepatitis C with a possibility of a cure.

Hepatitis C

NEW DAAs in the management of Hepatitis C

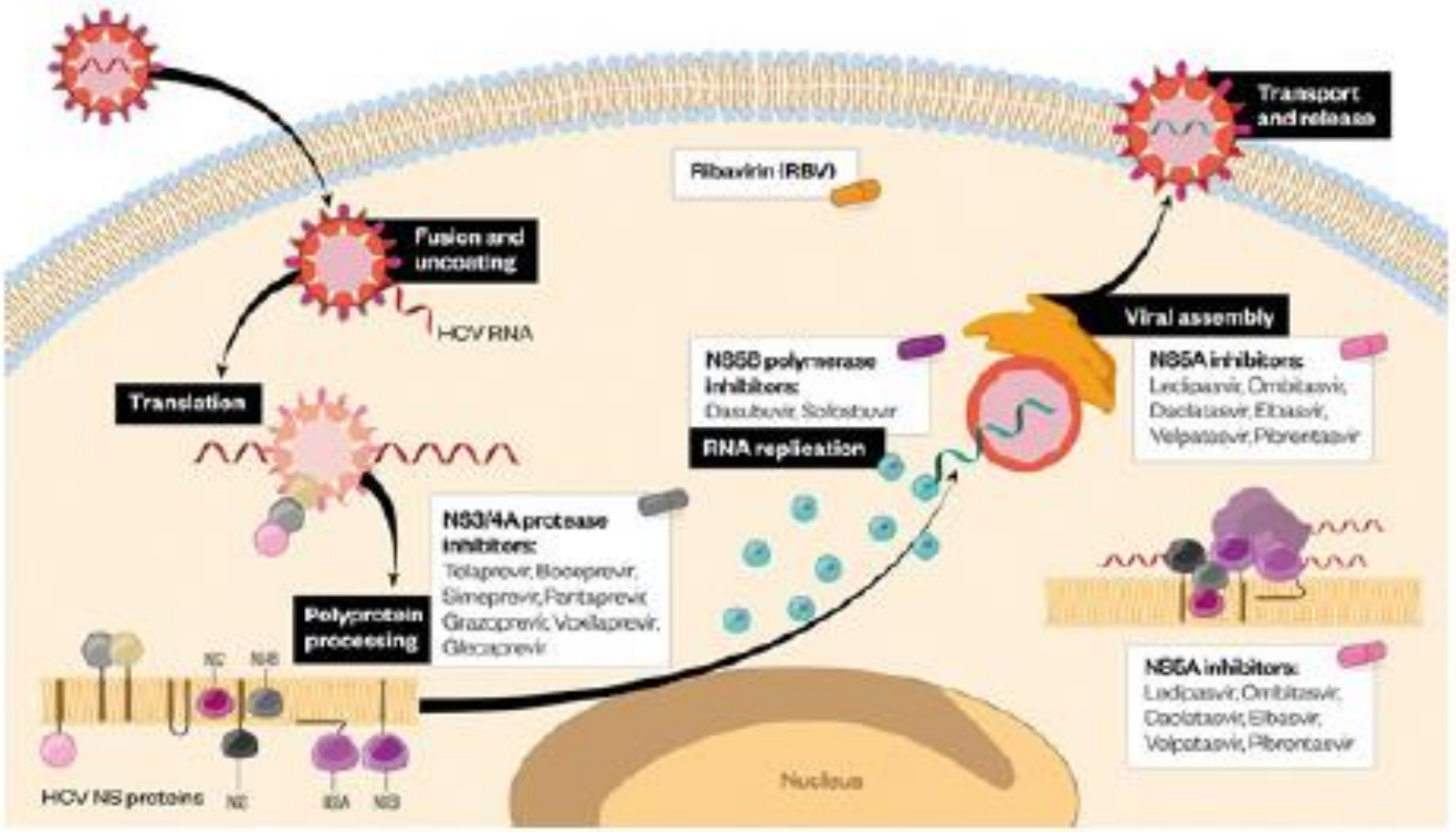
Classe	*Noms*	*Mécanisme d'action*	*Exemples*
Inhibiteurs de la protéase	-previr	Inhibent la protéase virale C NS3-4A	Telaprevir (Incivo®), boceprevir (Victrelis®), simeprevir (Olysio®)1, peritaprevir (Viekirax®)2, Asunaprevir, grazoprevir3
Inhibiteurs de la protéine NS5A	-asvir	Inhibent NS5A, une protéine virale C impliquée dans la réplication et la production de particules virales	Daclatasvir (Daklinza®)1, Ombitasvir (Viekirax®)2, Ledipasvir (Harvoni®)4, Elbasvir,GS5816
Inhibiteurs de la polymérase	-buvir	Inhibitent la polymérase virale C	Sofosbuvir (Sovaldi®), dasabuvir (Exviera®), Beclabuvir, MK36823

Hepatitis C

Site of Action of New Drugs

Protease Inhibitors	NS5A Inhibitors	NS5B Inhibitors
TELAPREVIR	DACLATASVIR	SOFOSBUVIR
BOCEPREVIR	LEDIPASVIR	DASABUVIR
SIMEPREVIR	OMBITASVIR	
VOXILAPREVIR	VELPATASVIR	
GLECAPREVIR	PIBRENTASVIR	

Hepatitis C virus life cycle and potential therapeutic targets



SOFOSBUVIR

- The first non interferon treatment for Hepatitis C.
- New treatment option for chronic Hepatitis C which offers hope of a cure.
- Hailed as a major breakthrough and game changer in the management of Hepatitis C.

SOFOSBUVIR

Key Facts

- NS5B nucleotide inhibitor. The NS5B RNA dependent polymerase is responsible for replication of Hepatitis C RNA.
- EMEA/FDA approval in late 2013/ beginning 2014 (marketed as Sovaldi).
- Oral administration as a 400mg tablet once daily
- Effective across all genotypes.
- Limited drug/drug interactions (as not metabolised by cytochrome P450).

SOFOSBUVIR

- Must be used in combination with ribavirin
- Can be used with or without peginterferon
- The combination therapy with sofosbuvir means a shorter duration of treatment from 24 to 12 weeks
- The clinical efficacy has been examined in a number of phase 3 clinical trials which included a proportion of difficult to treat populations, such as patients with cirrhosis
- Response rate can range from 56-97% depending on genotypes and protocol regimens

SOFOSBUVIR

- No side effects have been identified that are specific to sofosbuvir and during combination treatment the side effects were consistent with those expected for ribavirin/peginterferon.

SOFOSBUVIR

Regimen without Interferon-Alfa 24w vs., 12w vs. Placebo	Regimen with Interferon-Alfa SOF/PEG/RBV vs. Placebo
Fatigue 30% (38%) [24%]	Fatigue 30% [55%]
Headache 30% (24%) [20%]	Headache 36% [44%]
Nausea 13% (22%) [18%]	Nausea 34% [29%]
Insomnia 16% (15%) [4%]	Insomnia 25% [29%]
Pruritus 27% (11%) [8%]	Pruritus 17% [17%]
Anaemia 6% (10%) [0%]	Anaemia 21% [12%]
Asthenia 21% (6%)[3%]	Asthenia 5% [3%]
Chills 2% (2%) [1%]	Chills 17% [18%]
Influenza-like illness 6% (3%) [3%]	Influenza-like illness 16% [18%]

DOSE

- Dosing : one tablet (400mg daily) with concomittant ribavirin with or without peginterferon

- High cost drug. Mauritius benefits from an access price

SOFOSBUVIR + LEDIPASVIR COMBINATION

- A fixed dose combination of sofosbuvir 400mg + ledipasvir 90mg in a single tablet for once daily administration (marketed as Harvoni).
- EMEA approval in november 2014/ US FDA approval.
- Indicated for genotype 1,4,5,6 including co-infection with HIV.
- Recommended dose is once daily for 8, 12 or 24 weeks depending whether the patient has cirrhosis or has received treatment previously.

SOFOSBUVIR + LEDIPASVIR COMBINATION

- Peginterferon is not used with this treatment and ribavirin is only used in patients with cirrhosis.
- Overall the studies for this combination show a well tolerated regimen with drug interactions being very rare.

LATEST DRUGS

- Velpatasvir (400mg) + Sofosbuvir (400mg) in a single tablet regimen (Epclusa)
- HCV NS5A inhibitor / NS5B inhibitor combination
- Approved by US FDA in June 2016
- Pan-genotypic
- Indicated for the treatment of adults with genotype 1-6
- Dose: one tablet taken once daily with or without food.

VELPATASVIR + SOFOSBUVIR

- It is the first all oral, pan-genotypic single tablet regimen for chronic hepatitis C infection
- It was approved for 12 weeks in patients without cirrhosis or with compensated cirrhosis. In patients with decompensated cirrhosis, it should be used in combination with ribavirin.

VELPATASVIR + SOFOSBUVIR

- The approval of this combination represents an important step forward in the global effort to potentially eliminate HCV as it provide a safe, simple and effective cure for the majority of HCV patients.

Latest Drugs

- Glecaprevir + Pibrantasvir (Mavyret)

  (NS3/4A protease inhibitor) (NS5A Inhibitor)

  Pan-genotypic

  Approval in August 2017 by FDA

  Duration of treatment: 8-12 weeks

- Sofosbuvir + Velpatasvir + Voxilapevir (Vosevi)

  (NS5B inhibitor) (NS5A inhibitor) (NS3/4A Protease inhibitor)

  - Pan genotypic approved by FDA in August 2017.
  - Duration of treatment: 12 weeks

Factors to consider to decide which protocol of treatment to use

- Genotype
- Co infection with HIV/Co-morbidities
- Drug interactions (with HIV medications mainly)
- Without cirrhosis, compensated or decompensated cirrhosis
- Treatment naive or treatment experienced
- Extrahepatic manifestations
- Liver transplant
- Renal insufficiency or renal transplant

Protocols of treatment: AASLD, EASL

Hepatitis C/ Hepatitis B

- The new drugs used in the management of Hepatitis C can reactivate the Hepatitis B virus in patients.
- Recommendation that all patients treated with these drugs be tested for Hepatitis B before receiving treatment.
- Close monitoring of patients.

The introduction of directly acting oral anti-viral drugs for the management/treatment of hepatitis C represents a major breakthrough/advance in medicine as they are effective, safe and simple to take and thus represents a major hope of cure for many hepatitis C patients.

Access to treatment is a major challenge due to high price

WHO target is to eradicate Hepatitis C by 2030- affordability, access, screening, awareness campaigns, increased efficacy of drugs to target resistant strains.

5.

PrEP – HIV Prevention Strategy

Pre-exposure Prophylaxis (PrEP)

HIV Prevention

- Pre-exposure prophylaxis (PrEP) is a HIV prevention strategy that involves the use of anti-retrovirals taken by individuals who are HIV negative to reduce the risk of acquiring HIV.

PrEP

- The majority of clinical research has focused on a combination of tenofovir + emricitabine (Truvada).

- This combination taken as PrEP cannot prevent transmission of HIV to the person who is taking it but inhibits viral replication within their body, limiting the number of infected cells, allowing natural immune responses to eradicate these infected cells.

PrEP

- PrEP has been available in U.S since 2012.
- The evidence supporting its use is impressive, particularly when considering the meta analysis completed by WHO which demonstrated a 70% reduction in HIV infection with PrEP USE.
- Recommended by WHO as an HIV prevention strategy.
- PrEP is a cost effective health intervention
- Concerns have been raised that availability of PrEP could reduce condom use and influence rates of sexually transmitted infections and drug resistance.

PrEP

- Challenges

  -Funding

  -Selecting the target group/Screening

  -Adherence

PrEP

- When combined with condoms and other prevention methods, PrEP is a powerful HIV prevention tool.
- People who use PrEP must commit to take the drug everyday and seeing their healthcare provider every 3 months for follow up.
- Event driven protocol v/s daily dosing
- It is a game changing drug strategy in the management of the global HIV epidemic.

PrEP

- Daily v/s event driven protocol
- Daily:

  -Pros: evidence based and good efficacy in a variety of population

  -Cons: Adherence issues, frequent testing and monitoring, drug wastage during periods of low sexual risk, toxicity(bone/renal),drug resistance, costly

PrEP

- Daily v/s event driven protocol
- Event driven:

-Pros: less risk of resistance, less costly, less wastage, reduced monitoring requirements and toxicity

-Cons: Adherence issues, investigated in MSM population only

Miscellaneous

Management of atopic dermatitis: a new era

- Crisaborole (Phosphodiesterase inhibitor)-topical
- Dupilumab (monoclonal antibody)-injectable

Migraine – The CGRP story

- New class of drugs targeting the CGRP protein could be the first preventive treatment to hit the market.

Smart inhalers

- to give asthma patients more data on their condition.Blue tooth enabled

Smart insulin- Glucose responsive insulin

Valbenazine – new drug to treat tardive dyskinesia

Thank you