Understanding the Place Of Darunavir Ritonavir (800MG And 100MG) In Antiretroviral Therapy (ART)

CONTENTS

Background and Objective of the Survey

Background

Antiretroviral therapy (ART) has profoundly transformed the management of HIV/AIDS, turning what was once a fatal diagnosis into a manageable chronic condition. ART involves the combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease. Among the various classes of ARVs, protease inhibitors (PIs) play a critical role by inhibiting the protease enzyme, which is essential for the maturation of infectious virus particles.

Darunavir, often administered in combination with a low dose of ritonavir, represents one of the most potent PIs currently available. Ritonavir acts primarily as a pharmacokinetic enhancer by inhibiting the cytochrome P450 3A4 enzyme, which metabolizes many PIs, including darunavir. This inhibition results in increased plasma concentrations of darunavir, thereby enhancing its antiviral efficacy at lower doses and reducing the pill burden for patients.

The combination of darunavir and ritonavir (Darunavir/ritonavir) has been recommended by numerous HIV treatment guidelines due to its potent antiviral activity, high genetic barrier to resistance, and favorable clinical profile. It is particularly valuable in treatment-experienced patients who may have developed resistance to other PIs.

Darunavir (DRV)

Darunavir is a protease inhibitor (PI) that was first approved by the FDA in 2006. It is specifically designed to inhibit the HIV-1 protease, an enzyme crucial for the replication of the virus. By blocking this enzyme, darunavir prevents the virus from maturing and becoming infectious. This makes it highly effective in reducing the viral load in patients.

Ritonavir (RTV)

Ritonavir is also a protease inhibitor, but it is used in low doses as a pharmacokinetic enhancer rather than as a direct antiviral agent in most treatment regimens. Ritonavir inhibits the cytochrome P450 3A4 enzyme, which is responsible for the metabolism of many drugs, including protease inhibitors like darunavir. By inhibiting this enzyme, ritonavir increases the plasma concentration of darunavir, enhancing its efficacy and allowing for less frequent dosing—a critical factor in improving adherence to treatment.

Combination Therapy: Darunavir/Ritonavir

The combination of darunavir with ritonavir is commonly prescribed for both treatment-naïve and treatment-experienced HIV patients due to several advantages:

Enhanced Efficacy: The ritonavir-boosted darunavir regimen is highly potent against HIV, including strains that have become resistant to other protease inhibitors.

High Barrier to Resistance: Darunavir has a high genetic barrier to resistance. This means that multiple mutations in the HIV genome are necessary before the virus can bypass the drug's effects, making this combination an excellent choice for preventing the development of resistance.

Flexible Dosing: The combination allows for once-daily dosing, which simplifies the treatment regimen and helps improve adherence to the medication schedule.
Broad Clinical Approval: Darunavir/ritonavir is recommended by various health authorities and is included in many HIV treatment guidelines globally due to its robust clinical data supporting its efficacy and safety profile.

Objective

The primary objective of this study is to critically evaluate the placement and efficacy of Darunavir Ritonavir (800mg/100mg) within the context of antiretroviral therapy for HIV/AIDS. The study aims to:

1. Assess the clinical efficacy of Darunavir Ritonavir in both treatment-naïve and treatment-experienced patients, focusing on viral suppression, immune recovery, and the prevention of resistance development.
2. Evaluate the pharmacokinetic advantages of ritonavir-boosted darunavir, which include enhanced bioavailability and reduced dosing frequency.
3. Review the safety profile and tolerability of Darunavir Ritonavir, considering its long-term use in managing a chronic condition like HIV/AIDS.
4. Analyze the cost-effectiveness of incorporating Darunavir Ritonavir into ART regimens, particularly in resource-limited settings where the burden of HIV is highest.
5. Explore patient-centered outcomes, such as quality of life and adherence to therapy, which are crucial for the long-term success of any antiretroviral regimen.

Methodology of the Survey

Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Management Of Antiretroviral Therapy with Boosted Protease Inhibitors—Darunavir/Ritonavir

Introduction:

The human immunodeficiency virus (HIV) remains a significant public health challenge globally, affecting nearly 40 million people worldwide. Antiretroviral therapy (ART) has been pivotal in managing the infection, significantly enhancing the life expectancy and quality of life for those infected. ART's role extends beyond therapeutic management, significantly reducing the transmission rates of HIV, including mother-to-child transmission during pregnancy [1,2].

Highly active antiretroviral therapy (HAART), especially, has been instrumental in reducing viral loads and improving the immune response in HIV-positive individuals. However, the use of first-generation antiretrovirals has been associated with notable side effects [3,4]. Moreover, despite the efficacy of ART in controlling the virus and prolonging life, there are instances of therapeutic failures due to various factors like poor adherence, inadequate drug potency, and viral resistance [6].

Among the various antiretroviral medications, protease inhibitors (PIs) play a crucial role, with darunavir (DRV) being a key component when boosted with ritonavir (RTV). Darunavir, used in combination with a pharmacokinetic enhancer like ritonavir, has been a cornerstone in HIV treatment regimens due to its potency and high barrier to resistance. This combination is particularly effective in both treatment-naive and treatment-experienced patients, providing durable control over the virus [7].

Ritonavir acts as a booster by inhibiting the enzyme that metabolizes protease inhibitors, thereby increasing the efficacy of darunavir by enhancing its plasma concentration. This combination allows for improved viral suppression and reduced frequency of dosing, which can significantly enhance patient adherence to the treatment regimen.

This study focuses on understanding the use of darunavir boosted with ritonavir within ART regimens, examining its impact on pharmacokinetics, and discussing the management of treatment to optimize outcomes. The potent combination of darunavir and ritonavir highlights the evolution of ART and its ability to address the challenges of drug resistance and treatment efficacy in the ongoing fight against HIV/AIDS.

Antiretroviral (ARV) Medication

Antiretroviral (ARV) medications encompass a diverse array of drug classes targeted against HIV-1, including nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase inhibitors, protease inhibitors (PIs), and pharmacokinetic enhancers (boosters). These classes collectively

include around 30 active molecules, and their efficacy is often maximized through various fixed-dose combinations to improve adherence and simplify administration. Examples include fixed dual, triple, and quadruple combinations such as emtricitabine/tenofovir, COBI/DRV, and elvitegravir/COBI/emtricitabine/tenofovir, respectively.

- **Human Immunodeficiency Virus (HIV) Protease**

The HIV protease plays a crucial role in the virus's life cycle by cleaving the Gag and Gag-Pol polyproteins into mature, functional proteins necessary for viral replication. HIV protease is a homo dimeric aspartyl protease with each monomer containing 99 amino acids and a catalytic aspartic acid at position 25. Its activity is essential for viral maturation, making it a prime target for ARV drugs. The active site of the protease, covered by two flaps, must be accessible for substrate entry, which can be blocked to inhibit the enzyme's function.

- **Protease Inhibitors (PIs)**

Protease inhibitors are a key class of ARV drugs, with darunavir (DRV) and ritonavir (RTV) being notable examples. The first PI, ritonavir, was approved in 1996, followed by others including indinavir, nelfinavir, and darunavir. These inhibitors are primarily metabolized by the liver's cytochrome P450 (CYP450) system, particularly the CYP 3A4 enzyme, leading to a high potential for drug-drug interactions.

Ritonavir, while a potent PI itself, is commonly used in small doses as a pharmacokinetic enhancer due to its strong inhibitory effect on CYP 3A4. This booster effect increases the plasma levels and half-life of co-administered PIs like darunavir without significantly heightening side effects, enhancing the overall efficacy and durability of the HIV treatment regimen.

PIs function by blocking the activity of HIV protease, preventing the virus from maturing and assembling new viral particles. This blockade occurs at a late stage in the HIV replication process, after the virus has already utilized the host cell's mechanisms to produce long viral precursor proteins. Although HIV can still replicate in the presence of PIs, the resultant virions are immature and incapable of infecting new cells, significantly halting the spread of infection.

In conclusion, PIs such as darunavir, when boosted with ritonavir or cobicistat, represent a powerful component of ARV regimens, effectively disrupting HIV replication and contributing to the long-term management of HIV infection. This strategy underscores the importance of carefully managing drug interactions and side effects to optimize treatment outcomes for individuals living with HIV.

Pharmacokinetic Enhancers: Ritonavir (RTV)

In the realm of HIV treatment, pharmacokinetic enhancers like Cobicistat (COBI) and Ritonavir (RTV) play a pivotal role in enhancing the effectiveness of protease inhibitors (PIs) by inhibiting the CYP3A4 enzyme, thereby increasing the drug concentration and efficacy of the PIs. Both substances have similar roles but differ in their enzyme interaction profiles and clinical applications.

Ritonavir (RTV)

Ritonavir, known commercially as Norvir, is part of combination therapies like Kaletra (lopinavir/RTV). Introduced to the U.S. market on March 1, 1996, RTV became a cornerstone in the battle against HIV/AIDS, significantly reducing mortality rates from the disease. It functions not only as a protease inhibitor but also as a potent inhibitor of the cytochrome P450 3A4 enzyme, which enhances the pharmacokinetic profiles of other PIs used in combination therapies.

The molecular structure of RTV is complex, involving multiple functional groups that interact with various enzymes. It is primarily known for its action on CYP3A4 but also affects other cytochrome enzymes to varying degrees. This broad spectrum of interaction helps in managing the drug levels of co-administered medications, thus enhancing their therapeutic effects while also managing potential adverse reactions.

RTV is formulated as an oral solution and tablets, and it is prescribed in combination with other antiretrovirals to treat HIV-1 in adults and children over two years of age. It is particularly used as a booster in dosages of 100 mg, enhancing the efficacy of other PIs like Darunavir (DRV) by inhibiting their metabolism and extending their half-life in the plasma.

Protease Inhibitor—Darunavir

Darunavir (DRV) is a modern protease inhibitor (PI) with a robust profile for treating HIV-1. Below is a more detailed overview of its properties, mechanism, and usage:

1. Pharmacological Profile

Development and Approval: DRV was developed as a synthetic nonpeptide PI in 1988, approved in the United States in 2006, and in Europe in 2007. It was introduced for clinical use to provide a high genetic barrier to the onset of viral resistance and effective antiviral activity against HIV-1 strains resistant to other protease inhibitors.

- Molecular Characteristics:
  - Molecular weight: 547.7 g/mole
  - Solubility: 0.15 mg/mL
  - Plasma protein binding: 95%

2. Clinical Usage

-Indications: Since 2016, DRV has been recommended for children over three years of age, adolescents, and treatment-naive adults, as well as for critically ill patients infected with HIV-1.

- Dosage Forms: DRV is available as a 100 mg/mL oral suspension and as film-coated tablets in doses of 75, 150, 300, or 600 mg. It is often used in fixed-dose combinations with cobicistat (COBI) (e.g., 800 mg DRV/150 mg COBI).

- Administration Regimen: Typically administered once or twice daily, in combinations such as 800 mg DRV with 150 mg COBI or 100 mg ritonavir (RTV) once daily, or 600 mg DRV twice daily with 150 mg COBI or 100 mg RTV.

3. Mechanism of Action

- Inhibition of HIV-1 Protease: DRV inhibits the dimerization and catalytic activity of HIV-1 protease, a critical enzyme necessary for the viral life cycle. By inhibiting this enzyme, DRV prevents the proteolytic cleavage of HIV-encoded Gag-Pol polyproteins, essential for the assembly of mature infectious viral particles.

- Impact on Viral Replication: DRV selectively inhibits the cleavage of Gag-Pol-encoded HIV polyproteins in virus-infected cells, thereby preventing the formation of infectious mature viral particles.

4. Pharmacodynamic Properties

-Efficacy and Safety: The efficacy and safety of DRV, alone or in combination with potentiating drugs like RTV or COBI, have been validated through extensive clinical trials. DRV significantly improves virological and immunological outcomes compared to other PIs and exhibits low cytotoxicity.

-Resistance Profile: DRV was designed to have a high genetic barrier against the development of resistance. It retains activity against wild-type HIV-1 and a wide range of viruses resistant to other PIs.

5. Therapeutic Advantages

- Reduced Viral Load: Clinical trials, such as the PARADIGM-HF study, have demonstrated that DRV can significantly reduce N-terminal B-type natriuretic peptide levels and improve left ventricular ejection fraction (LVEF), offering more clinical and symptomatic benefits compared to ACEI/ARB.

Role in HAART: DRV has become a vital component of Highly Active Antiretroviral Therapy (HAART), especially in patients with resistance to other PIs or those requiring a robust regimen due to severe disease states.

DRV's introduction marked a significant advancement in HIV treatment, offering a durable option with potent antiviral effects, especially in patients harboring resistant viral strains or those requiring intensive therapeutic management.

Conclusions and Future Directions

The advent of protease inhibitors (PIs) marked a significant advance in the management of HIV, improving patient outcomes dramatically. Newer generations of PIs, such as darunavir (DRV), are well-tolerated and have transformed the therapeutic landscape with their high efficacy, safety, and reduced pill burden, enhancing patient compliance.

Darunavir (DRV) and Ritonavir (RTV):
- Efficacy and Resistance: DRV is highly effective against both wild-type HIV and resistant strains. It is commonly co-administered with a pharmacokinetic booster like ritonavir (RTV) or cobicistat (COBI), enhancing its pharmacokinetic profile. This combination has shown to increase the barrier against viral resistance and provide specific immune benefits.

- **Pharmacokinetic Enhancers:** Both RTV and COBI act as boosters by inhibiting the metabolic pathways that break down drugs like DRV, thus enhancing their effectiveness. While they have similar effects on inhibiting enzymes like CYP3A4 and enhancing drug exposure, there are subtle differences in their interaction profiles with other drugs and inducers that may affect their effectiveness.

- **Administration and Tolerability:** Boosted DRV, particularly with RTV, is noted for its tolerability and reduced side effects compared to other regimens. This makes DRV with RTV a viable treatment option for both treatment-naive and experienced patients.

- **Clinical Implications:** Due to the critical role of pharmacokinetic enhancers in the effectiveness of DRV, clinicians need to be aware of the potential drug interactions, especially in patients with multiple comorbidities. Monitoring and adjusting treatment regimens as needed is crucial to maintain therapeutic efficacy and manage side effects effectively.

In conclusion, DRV, particularly when boosted with RTV, continues to be a cornerstone in the fight against HIV, offering significant advantages in terms of potency, patient adherence, and a high barrier to resistance.

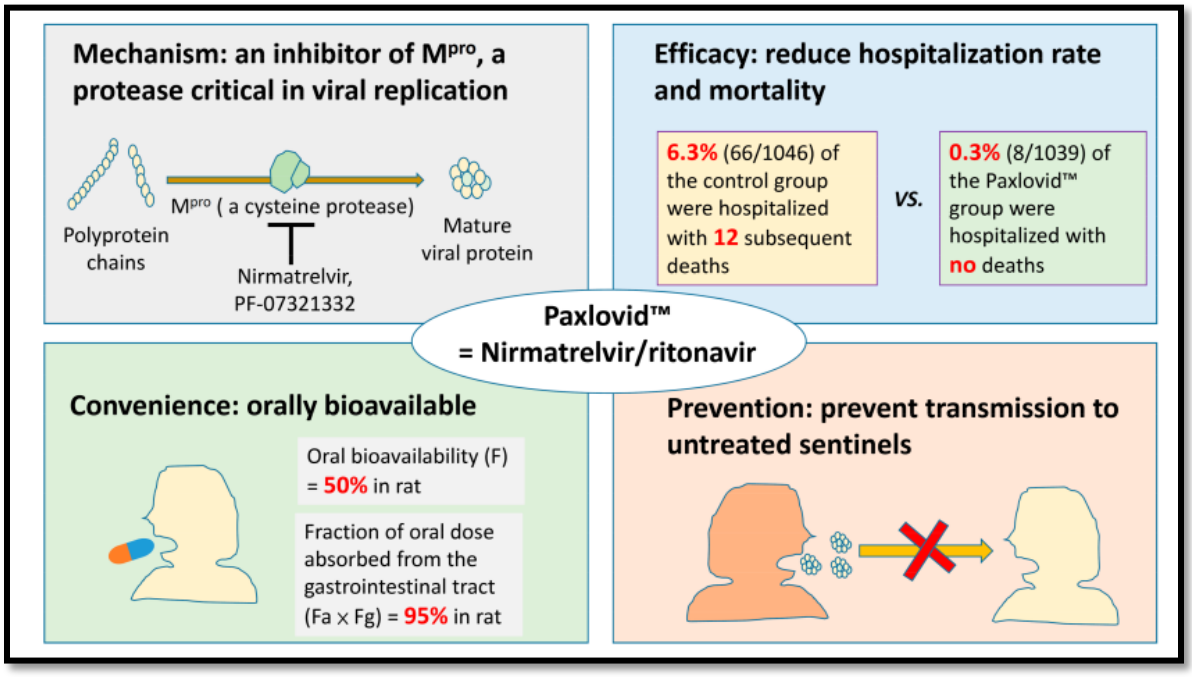
Oral Ritonavir Therapy for COVID-19: The Dawn in the Dark?

Introduction to Ritonavir in COVID-19 Treatment

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has led to devastating global health and economic impacts. As of December 2021, the virus has claimed over 5.5 million lives with more than 272 million cases reported worldwide. The emergence of new variants, including the highly transmissible Omicron variant, underscores the urgent need for effective therapeutic interventions. Among various treatments explored, the combination of nirmatrelvir and ritonavir has shown promising results in reducing hospitalizations and deaths associated with COVID-19.

Role of Ritonavir in Enhancing Nirmatrelvir's Efficacy

Ritonavir, primarily known for its use in treating HIV, plays a crucial role in the therapeutic regimen against SARS-CoV-2 by enhancing the effectiveness of nirmatrelvir. It does so by inhibiting the CYP3A4 enzyme, a liver enzyme responsible for the metabolism of many drugs. This inhibition increases the plasma concentration of nirmatrelvir, thereby amplifying its antiviral effects against SARS-CoV-2.



Mechanism and Impact

The combination of nirmatrelvir/ritonavir, marketed as Paxlovid™, targets the main protease (Mpro) of the virus, which is essential for viral replication. By inhibiting this protease, the drug prevents the virus from replicating within the host cells. Clinical trials have demonstrated that nirmatrelvir/ritonavir can reduce the risk of hospitalization or death by 89% when administered early in the course of the infection.

Clinical Trials and Approvals

Nirmatrelvir/ritonavir has been evaluated in various clinical trials, leading to its Emergency Use Authorization (EUA) by the FDA in December 2021 for high-risk, non-hospitalized patients. This approval underscores the combination's potential in altering the course of the pandemic by providing an effective early treatment option.

Pharmacokinetic Properties

The pharmacokinetic profile of ritonavir in combination with nirmatrelvir shows a synergistic effect, enhancing the bioavailability and efficacy of the treatment. Ritonavir's peak concentration time and half-life ensure sustained drug levels in the system, crucial for effective viral suppression.

Safety and Side Effects

While ritonavir is effective in boosting nirmatrelvir's antiviral activity, it is also associated with several side effects such as gastrointestinal disturbances and liver enzyme elevations. These are generally manageable and are a trade-off for the benefits provided in combating COVID-19.

Conclusion

In conclusion, the strategic use of ritonavir to enhance nirmatrelvir's antiviral capacity represents a significant advancement in the treatment of COVID-19. This combination therapy not only reduces the severity of the disease but also decreases the overall burden on healthcare systems. Ongoing research and real-world data will continue to define its role in managing COVID-19, particularly against emerging variants.

Efficacy And Safety of Ritonavir In COVID-19: A Systematic Review of Randomized Controlled Trials

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has necessitated urgent therapeutic interventions. Among repurposed drugs, ritonavir, known for its use in HIV treatment, has been administered for COVID-19 due to its inhibitory action on viral proteases. Given the critical need for effective COVID-19 treatments, evaluating the efficacy and safety of ritonavir is essential.

Methods

Study Identification: Databases such as PubMed, medRxiv, and others were searched up to December 27, 2020, for randomized controlled trials assessing the efficacy and safety of ritonavir in COVID-19.

Selection Criteria: Included were randomized controlled trials involving COVID-19 patients treated with ritonavir, with or without comparisons to other interventions like placebo or supportive care. Exclusion criteria encompassed non-randomized studies, in vitro or animal studies, and those with fewer than ten participants.

Data Synthesis: Mortality and therapeutic outcomes were pooled as risk differences, and virological and radiological outcomes as risk ratios using a random-effects model. Heterogeneity was assessed using the I^2 statistic.

Results

Study Characteristics: The search yielded seven trials varying in control interventions and methodologies, with a total of 82 full-text articles assessed for eligibility.
Efficacy Outcomes: Ritonavir did not significantly reduce mortality compared to supportive care (RD: 0.00, 95% CI: -0.01 to 0.02). Similar trends were observed for virological cure (RR: 1.06, 95% CI: 0.85 to 1.31) and radiological improvements (RR: 0.81, 95% CI: 0.62 to 1.05).
Safety Profile: A significant increase in adverse events was noted with ritonavir compared to other interventions (RR: 2.96, 95% CI: 1.42 to 6.18), indicating a higher risk profile which necessitates careful clinical consideration.

Discussion

The use of ritonavir in COVID-19 does not confer benefits in reducing mortality, improving virological clearance, or radiological outcomes. The heightened risk of adverse events underscores the need for cautious use. These findings align with ritonavir's known pharmacodynamic properties and its interactions within the protease inhibition pathways.

Conclusion

The incorporation of ritonavir into COVID-19 treatment protocols does not improve clinical outcomes and is associated with a substantial increase in adverse events. Given the lack of significant benefits and the potential for harm, the use of ritonavir should be critically evaluated in ongoing and future clinical trials. Further research is needed to establish a robust evidence base for the use of ritonavir in COVID-19, preferably through well-designed, randomized controlled trials.

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- Darunavir (DRV) is an HIV protease inhibitor commonly used as part of antiretroviral treatment regimens globally for children and adolescents. It requires a pharmacological booster, such as ritonavir (RTV) or cobicistat. To better understand the pharmacokinetics (PK) of DRV in this younger population and the importance of the RTV boosting effect, a population PK sub study was conducted within SMILE trial, where the maintenance of HIV suppression with once daily integrate inhibitor + darunavir/ritonavir in children and adolescents is evaluated.
- A joint population PK model that simultaneously used total DRV, unbound DRV, and total RTV concentrations was developed. Competitive and non-competitive models were examined to define RTV's influence on DRV pharmacokinetics.
- Linear and non-linear equations were tested to assess DRV protein binding. A total of 443 plasma samples from 152 adolescents were included in this analysis. Darunavir PK was best described by a one-compartment model first-order absorption and elimination. The influence of RTV on DRV pharmacokinetics was best characterized by ritonavir area under the curve on DRV clearance using a power function.
- The association of non-linear and linear equations was used to describe DRV protein binding to alpha-1 glycoprotein and albumin, respectively. In our population, simulations indicate that 86.8% of total and unbound DRV trough concentrations were above 0.55 mg/L [10 times protein binding-adjusted EC_{50} for wild-type (WT) HIV-1] and 0.0243 mg/L (10 times EC_{90} for WT HIV-1) targets, respectively.
- Predictions were also in agreement with observed outcomes from adults receiving 800/100 mg DRV/r once a day. Administration of 800/100 mg of DRV/r once daily provides satisfactory concentrations and exposures for adolescents aged 12 years and older.

SURVEY FORM

1. In your clinical practice, how many patients are newly diagnosed with HIV in a month?

A. <5

B. 5 - <20

C. 20 - <30

D. ≥ 35

2. In your opinion, the incidence of HIV in Indian patients is higher in which age group?

A. < 18 years

B. 18-65 years

C. > 65 years

3. In your clinical practice, which is the most common opportunistic infections (OIs) presenting in patients living with HIV?

A. TB (including pulmonary and extra-pulmonary)

B. Candidiasis

C. Diarrhea

D. Herpes zoster

4. In your clinical practice, how often do you monitor CD4 count in patients living with HIV?

A. At every 3 months

B. At every 6 months

C. At every 12 months

5. In your clinical practice, which is the preferred boosted protease inhibitor?

A. Atazanavir/ ritonavir

B. Lopinavir/ ritonavir

C. Darunavir/ ritonavir

6. According to NACO, advanced HIV disease in adults, adolescents and children more than 5 years is referred to as

A. CD4 cell count <50 cells/mm3

B. CD4 cell count <100 cells/mm3

C. CD4 cell count <200 cells/mm3

D. CD4 cell count <300 cells/mm

7. According to NACO, in clinically asymptomatic individuals, for the HIV testing and diagnosis in adults and children above the age of 18 months

A. The sample should be reactive with one kit

B. The sample should be reactive with two different kits

C. The sample should be reactive with three different kits

D. The sample should be reactive with four different kits

8. According to your opinion, what are the benefits of prescribing fixed-dose combinations (FDCs) in ART?

A. They are easy to prescribe

B. Easy for patients to take, thereby improved and desirable adherence.

C. To minimize development of drug-resistant mutants hence reduce treatment failure

9. In your opinion, which drug has the highest genetic barrier to resistance?

A. Atazanavir/ ritonavir

B. Lopinavir/ ritonavir

C. Darunavir/ ritonavir

10. In your clinical practice, which is the preferred HIV patient profile for the ART containing Darunavir/Ritonavir (800/100 mg once daily)?

A. For the treatment of naive patients

B. For the treatment of experienced patients

11. According to your expert opinion, what are the potential advantages of DRV/r (800/100) have advantages over DRV/r (600/100)?

A. Higher efficacy

B. Fewer chances of drug resistance

C. Better tolerability

12. In your clinical practice, which is/ are the most common adverse effect/s observed with Darunavir therapy?

A. Hepatotoxicity

B. Skin rash

C. Diarrhoea

D. Headache

13. In your clinical practice, which is the preferred Darunavir and Ritonavir combination?

A. Once-daily Darunavir 800 mg and Ritonavir 100 mg

B. Twice-daily Darunavir 600 mg and Ritonavir 100 mg

14. In your opinion, what are the potential advantages of Ritonavir-boosted Darunavir combination?

A. Increases drug exposure and prolongs DRV half-life

B. Leads to a highest genetic barrier to resistance

C. DRV/r well tolerated and has a lipid profile more favorable than that of ritonavir-boosted lopinavir in terms of total cholesterol and triglyceride changes

15. In your clinical practice, how would you rate the compliance of Darunavir/Ritonavir (800/100) in ART?

A. Excellent

B. Better

C. Good

D. Poor

SURVEY FINDINGS

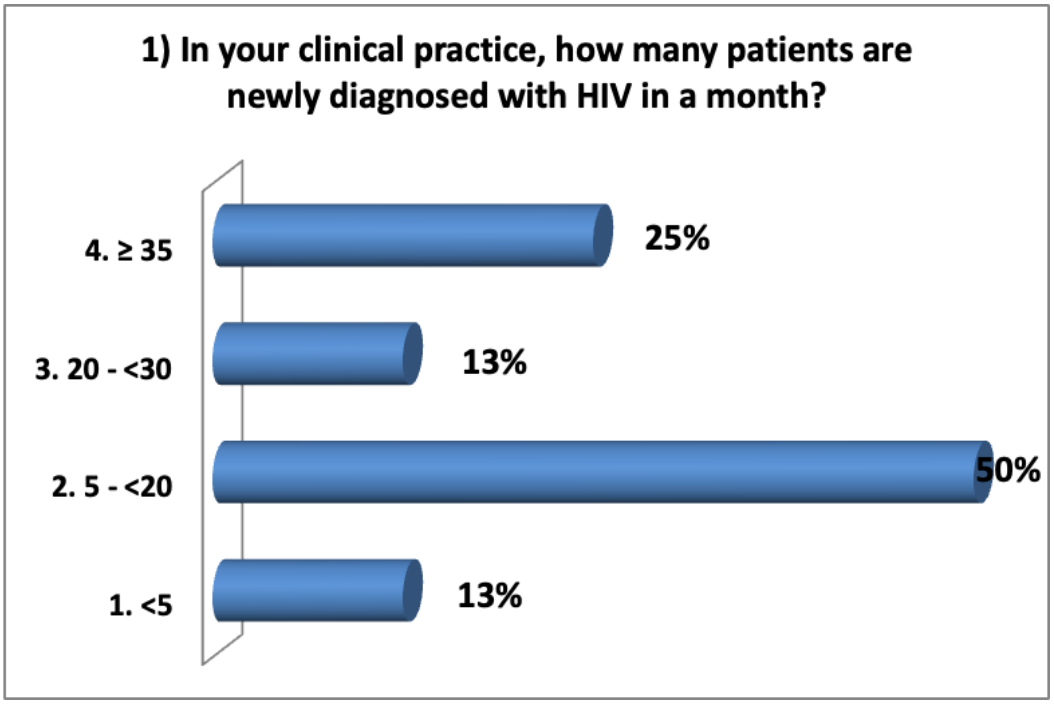
1. In your clinical practice, how many patients are newly diagnosed with HIV in a month?

A. <5

B. 5 - <20

C. 20 - <30

D. ≥ 35



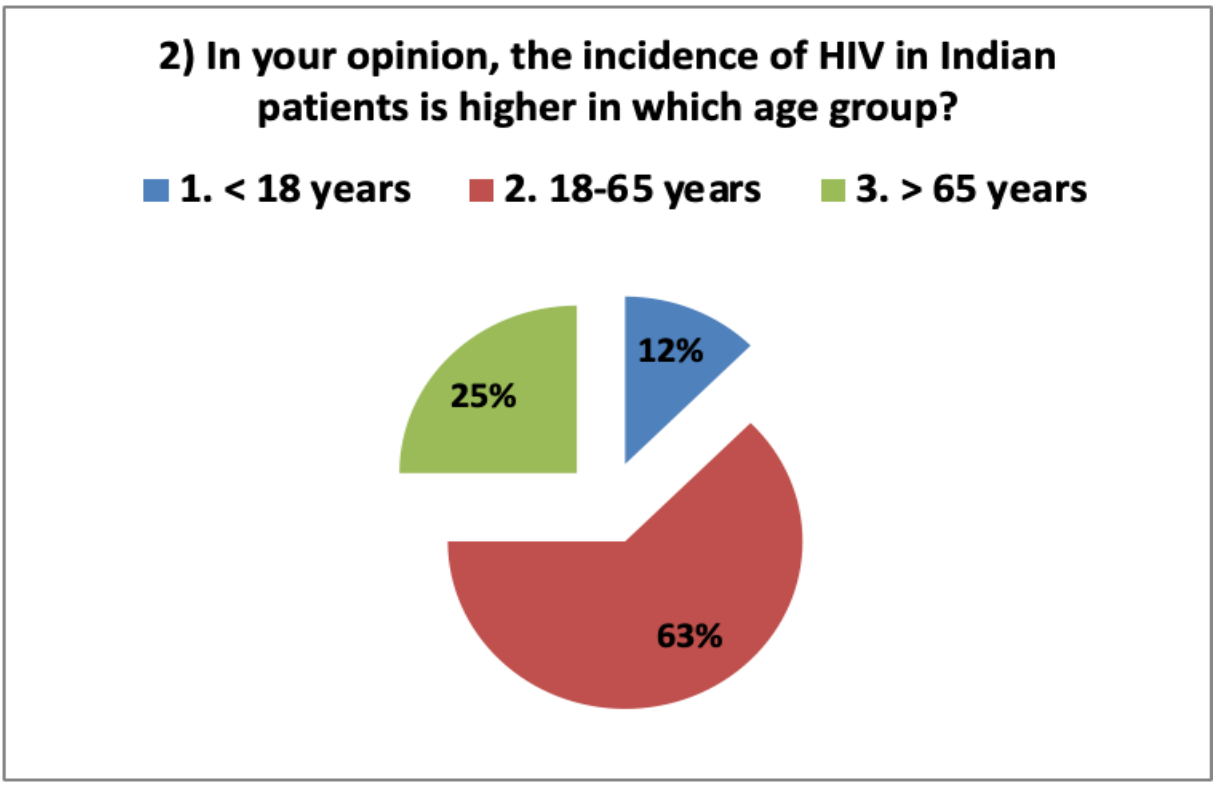
In the clinical practice, 5 to <20 patients are newly diagnosed with HIV in a month.

2. In your opinion, the incidence of HIV in Indian patients is higher in which age group?

A. < 18 years

B. 18-65 years

C. > 65 years



In the opinion, the incidence of HIV in Indian patients is higher in the 18-65 years age group.

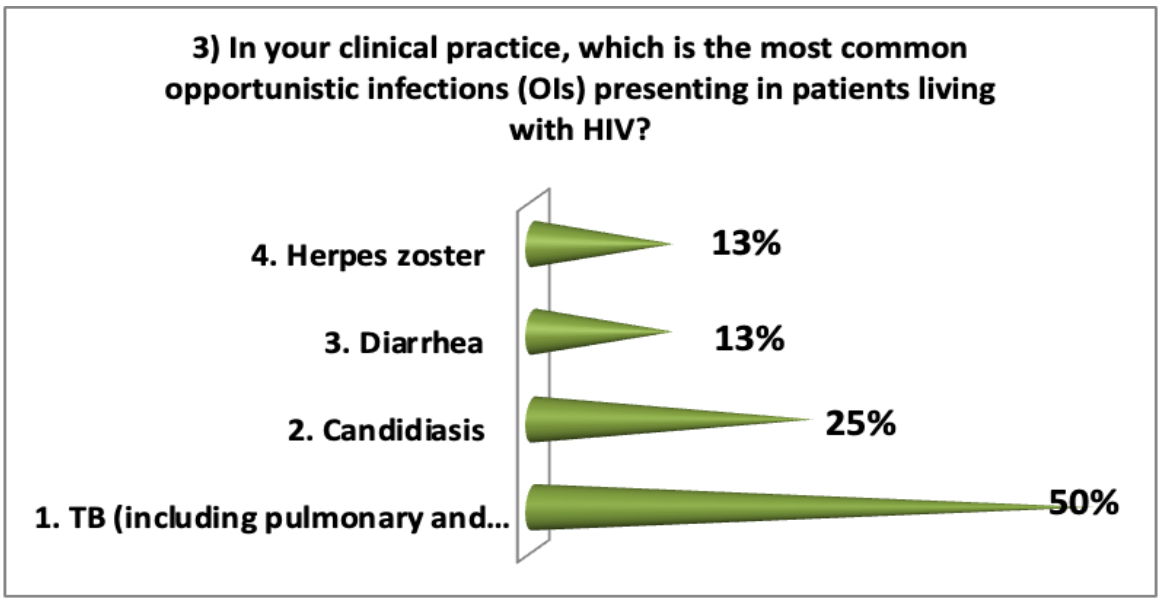
3. In your clinical practice, which is the most common opportunistic infections (OIs) presenting in patients living with HIV?

A. TB (including pulmonary and extra-pulmonary)

B. Candidiasis

C. Diarrhea

D. Herpes zoster



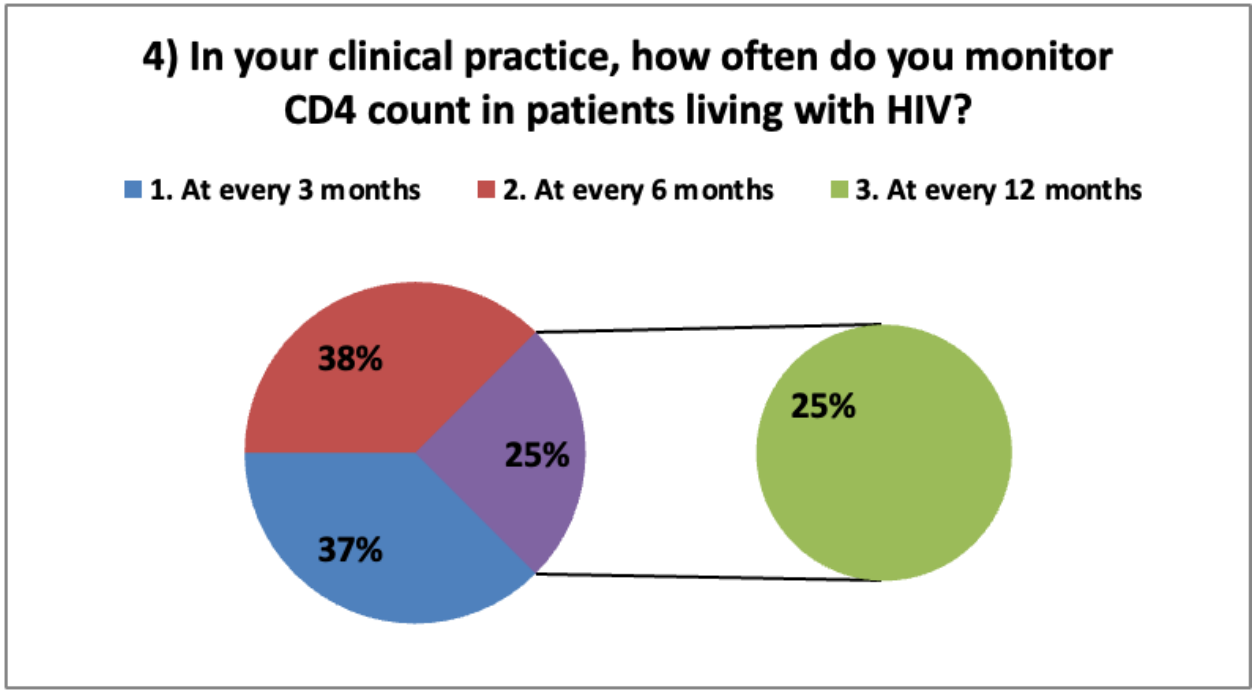
In the clinical practice, the most common opportunistic infection presenting in patients living with HIV is TB (including pulmonary and extra-pulmonary), as reported by 50% of respondents.

4. In your clinical practice, how often do you monitor CD4 count in patients living with HIV?

A. At every 3 months

B. At every 6 months

C. At every 12 months



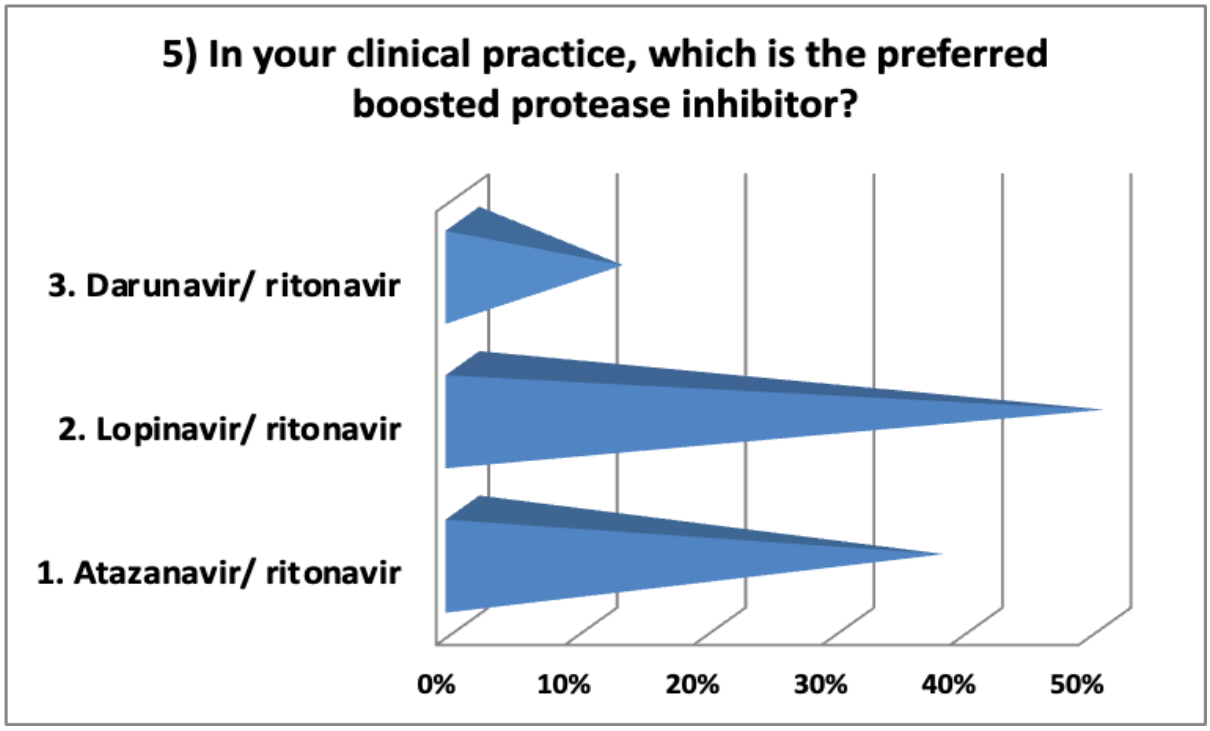
In the clinical practice, CD4 count was monitor in patients living with HIV every 6 months.

5. In your clinical practice, which is the preferred boosted protease inhibitor?

A. Atazanavir/ ritonavir

B. Lopinavir/ ritonavir

C. Darunavir/ ritonavir



In our clinical practice, the preferred boosted protease inhibitor is Lopinavir/ritonavir.

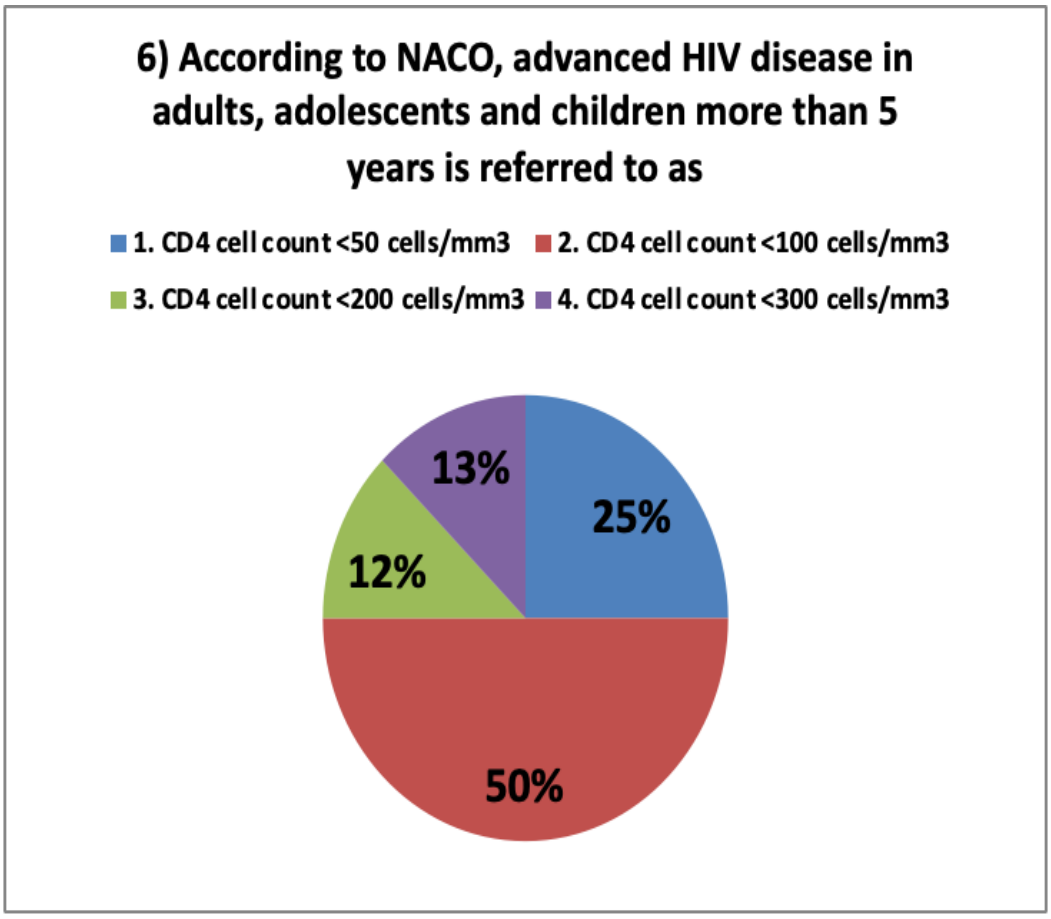
6. According to NACO, advanced HIV disease in adults, adolescents and children more than 5 years is referred to as

A. CD4 cell count <50 cells/mm3

B. CD4 cell count <100 cells/mm3

C. CD4 cell count <200 cells/mm3

D. CD4 cell count <300 cells/mm3



According to NACO, advanced HIV disease in adults, adolescents and children more than 5 years is referred to as a CD4 cell count <100 cells/mm^3.

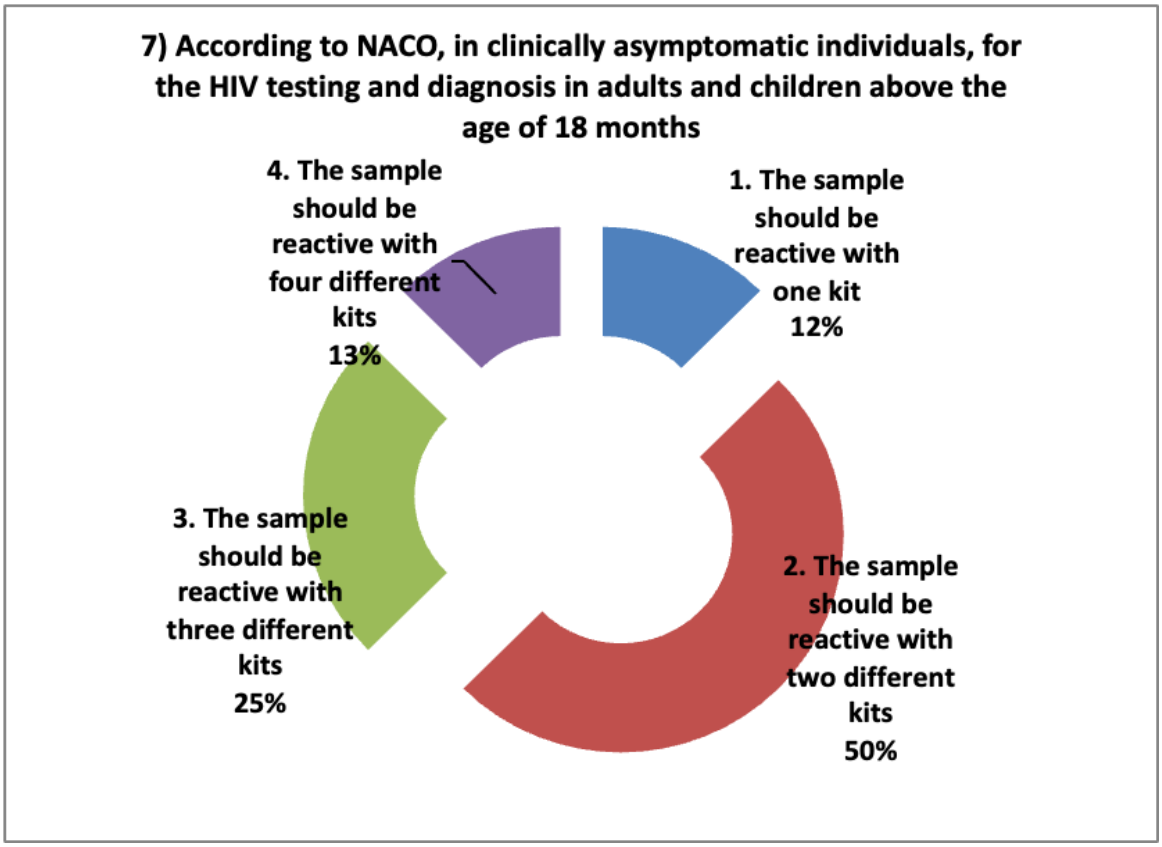
7. According to NACO, in clinically asymptomatic individuals, for the HIV testing and diagnosis in adults and children above the age of 18 months

A. The sample should be reactive with one kit

B. The sample should be reactive with two different kits

C. The sample should be reactive with three different kits

D. The sample should be reactive with four different kits



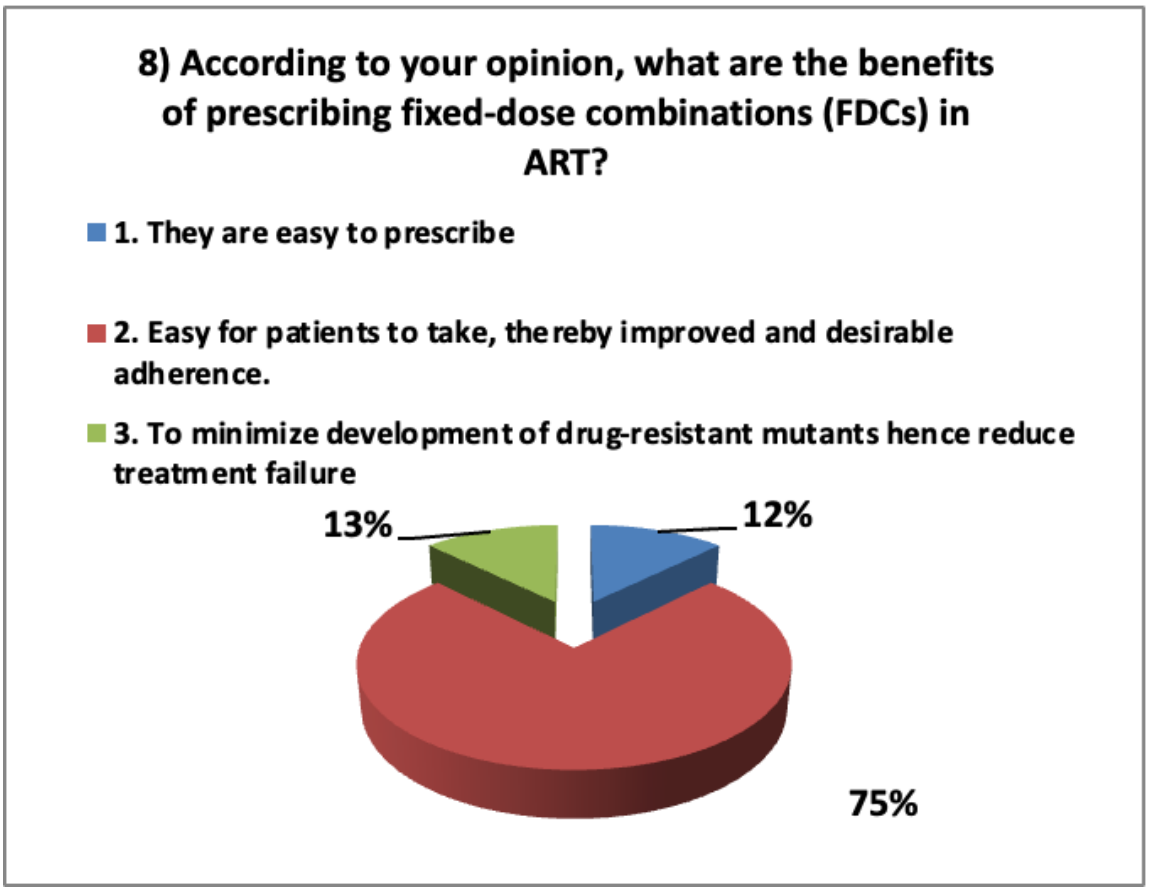
According to NACO, in clinically asymptomatic individuals, for HIV testing and diagnosis in adults and children above the age of 18 months, the sample should be reactive with two different kits.

8. According to your opinion, what are the benefits of prescribing fixed-dose combinations (FDCs) in ART?

A. They are easy to prescribe

B. Easy for patients to take, thereby improved and desirable adherence.

C. To minimize development of drug-resistant mutants hence reduce treatment failure



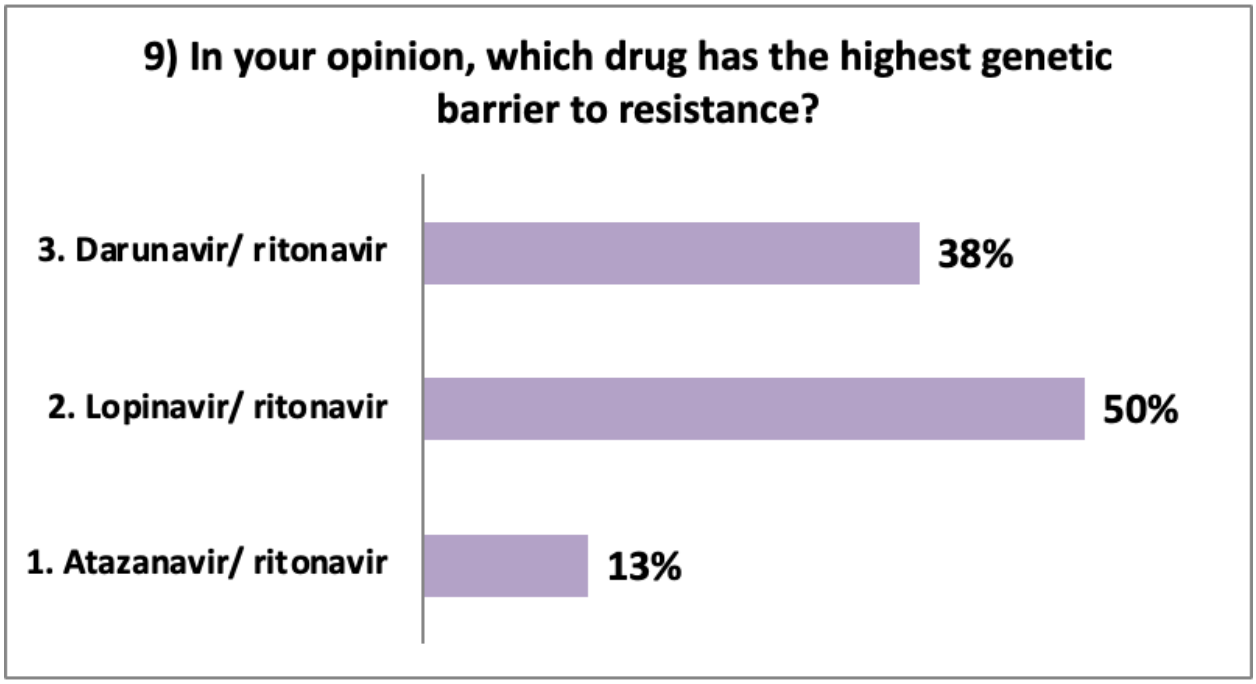
In the opinion, the primary benefit of prescribing fixed-dose combinations (FDCs) in ART is that they are easy for patients to take, thereby improving and promoting desirable adherence.

9. In your opinion, which drug has the highest genetic barrier to resistance?

A. Atazanavir/ ritonavir

B. Lopinavir/ ritonavir

C. Darunavir/ ritonavir

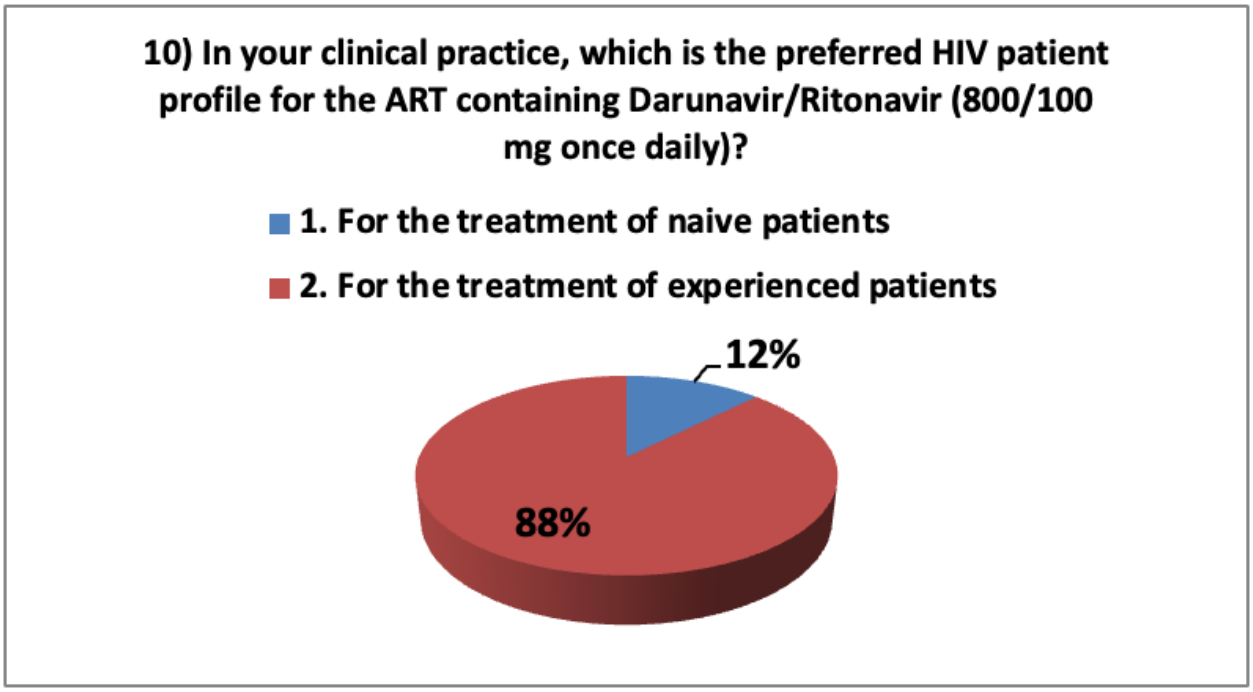


In the opinion, Lopinavir/ ritonavir has the highest genetic barrier to resistance.

10. In your clinical practice, which is the preferred HIV patient profile for the ART containing Darunavir/Ritonavir (800/100 mg once daily)?

A. For the treatment of naive patients

B. For the treatment of experienced patients



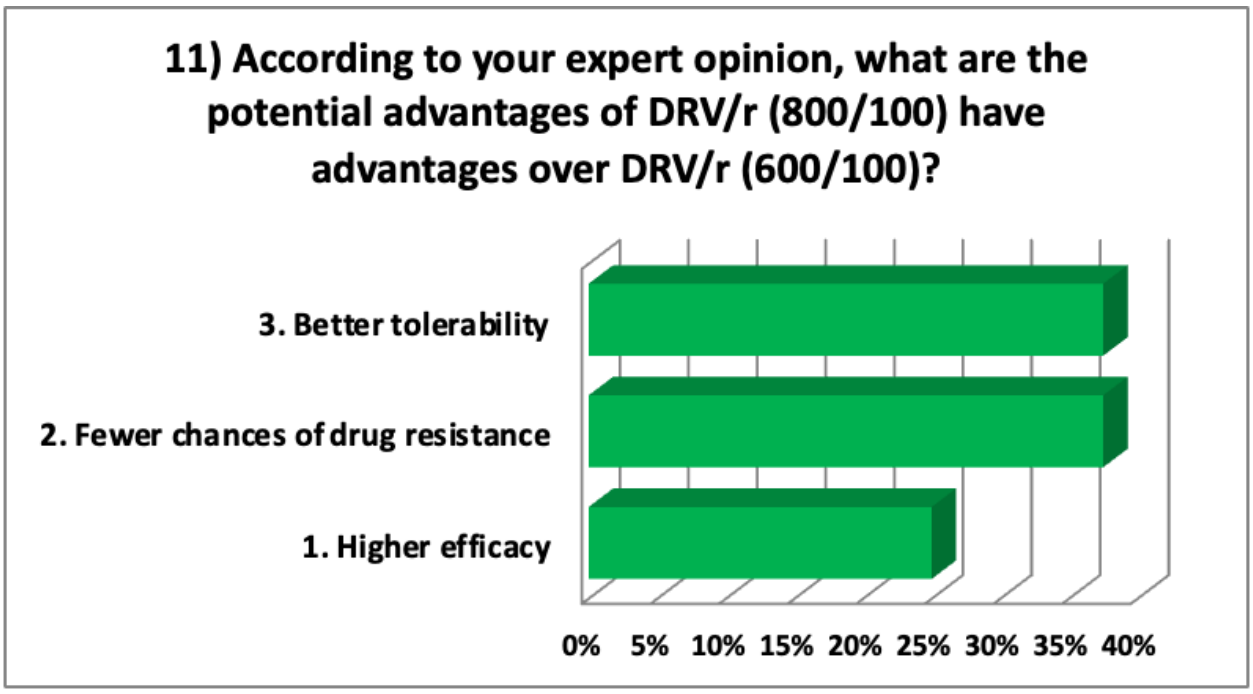
The preferred HIV patient profile for the ART containing Darunavir/Ritonavir (800/100 mg once daily) is for the treatment of experienced patients.

11. According to your expert opinion, what are the potential advantages of DRV/r (800/100) have advantages over DRV/r (600/100)?

A. Higher efficacy

B. Fewer chances of drug resistance

C. Better tolerability



In expert opinion, DRV/r (800/100) has potential advantages over DRV/r (600/100) in terms of fewer chances of drug resistance and better tolerability.

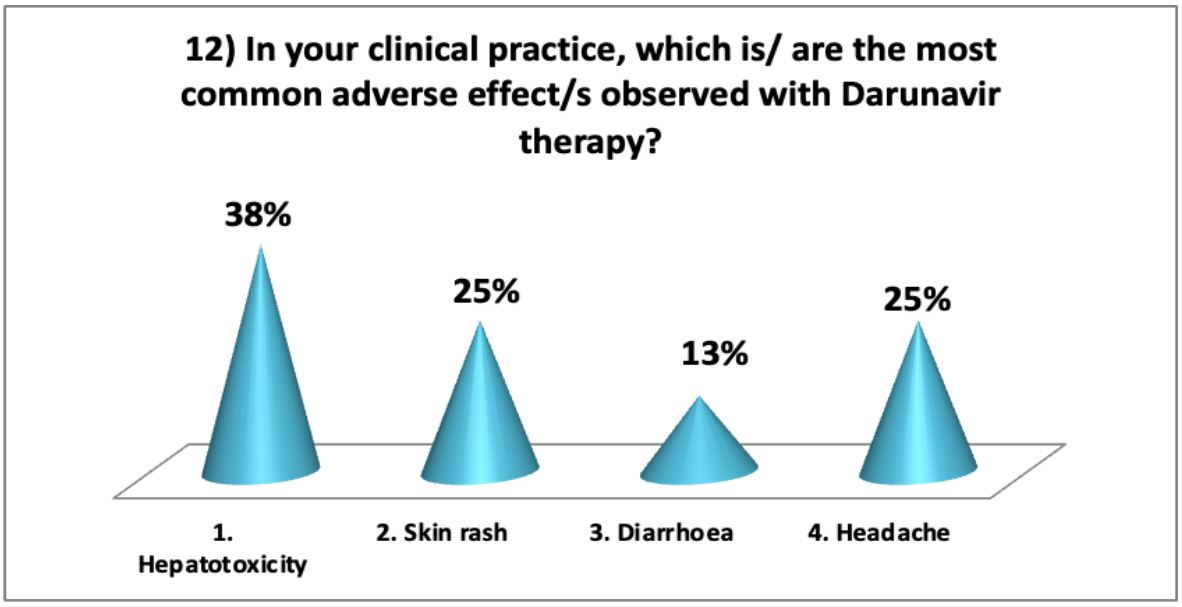
12. In your clinical practice, which is/ are the most common adverse effect/s observed with Darunavir therapy?

A. Hepatotoxicity

B. Skin rash

C. Diarrhoea

D. Headache

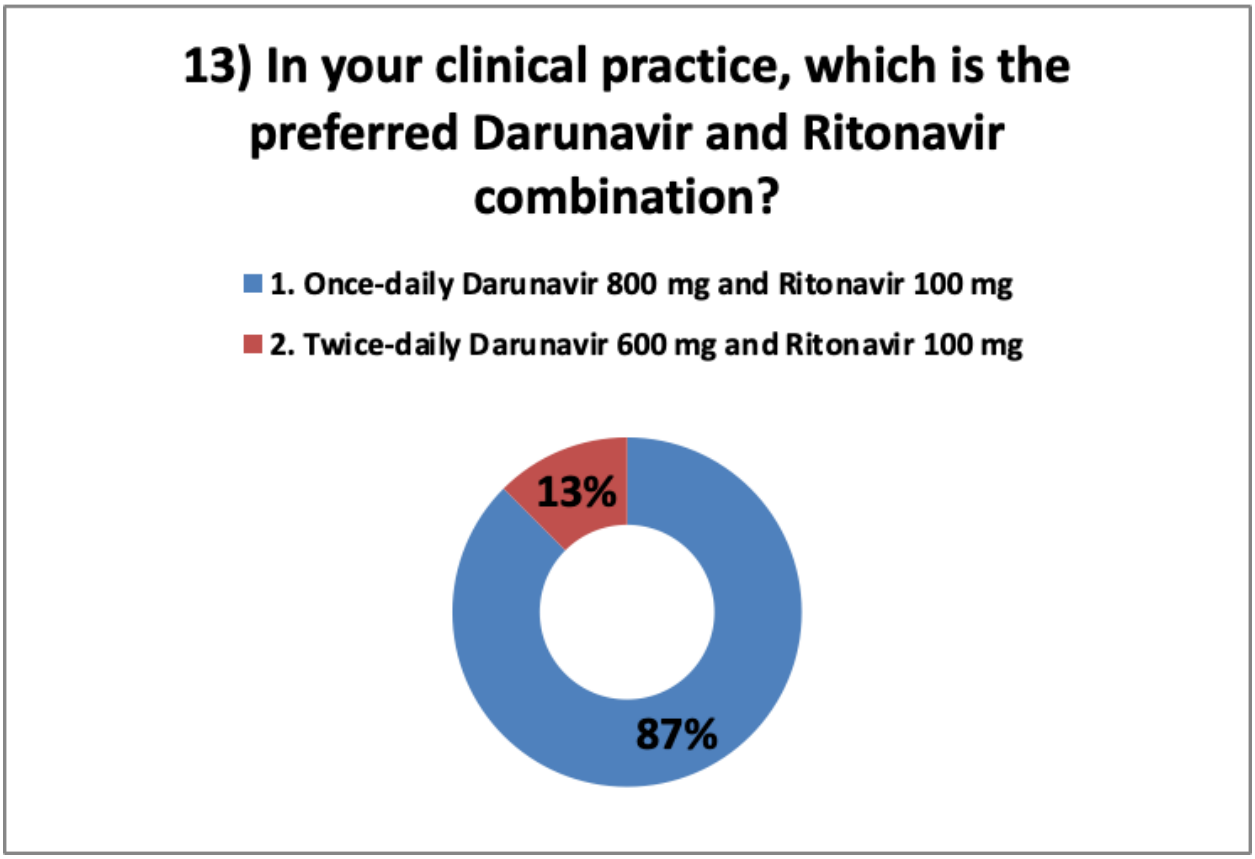


In the clinical practice, the most common adverse effect observed with Darunavir therapy is hepatotoxicity, as reported by 38% of respondents.

13. In your clinical practice, which is the preferred Darunavir and Ritonavir combination?

A. Once-daily Darunavir 800 mg and Ritonavir 100 mg

B. Twice-daily Darunavir 600 mg and Ritonavir 100 mg



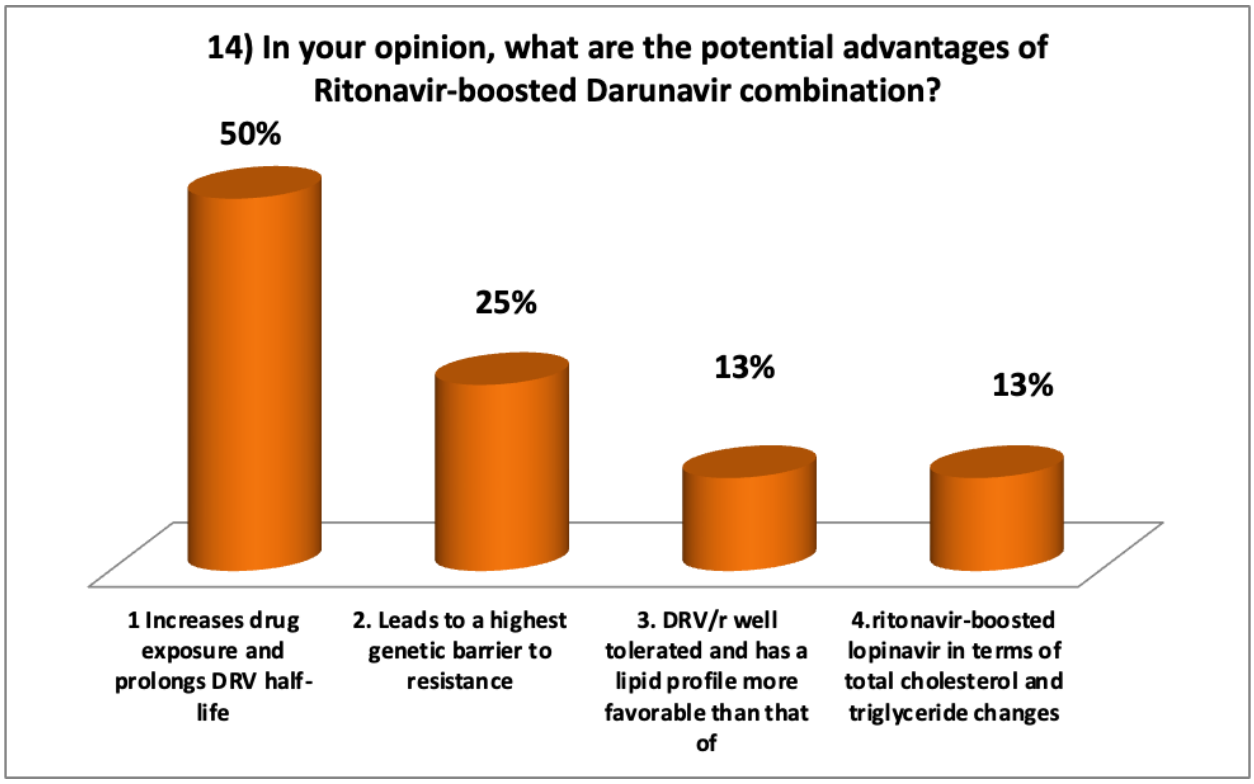
In the clinical practice, the preferred Darunavir and Ritonavir combination is once-daily Darunavir 800 mg and Ritonavir 100 mg.

14. In your opinion, what are the potential advantages of Ritonavir-boosted Darunavir combination?

A. Increases drug exposure and prolongs DRV half-life

B. Leads to a highest genetic barrier to resistance

C. DRV/r well tolerated and has a lipid profile more favorable than that of ritonavir-boosted lopinavir in terms of total cholesterol and triglyceride changes



In my opinion, the potential advantages of Ritonavir-boosted Darunavir combination include increases drug exposure and prolongs DRV half-life

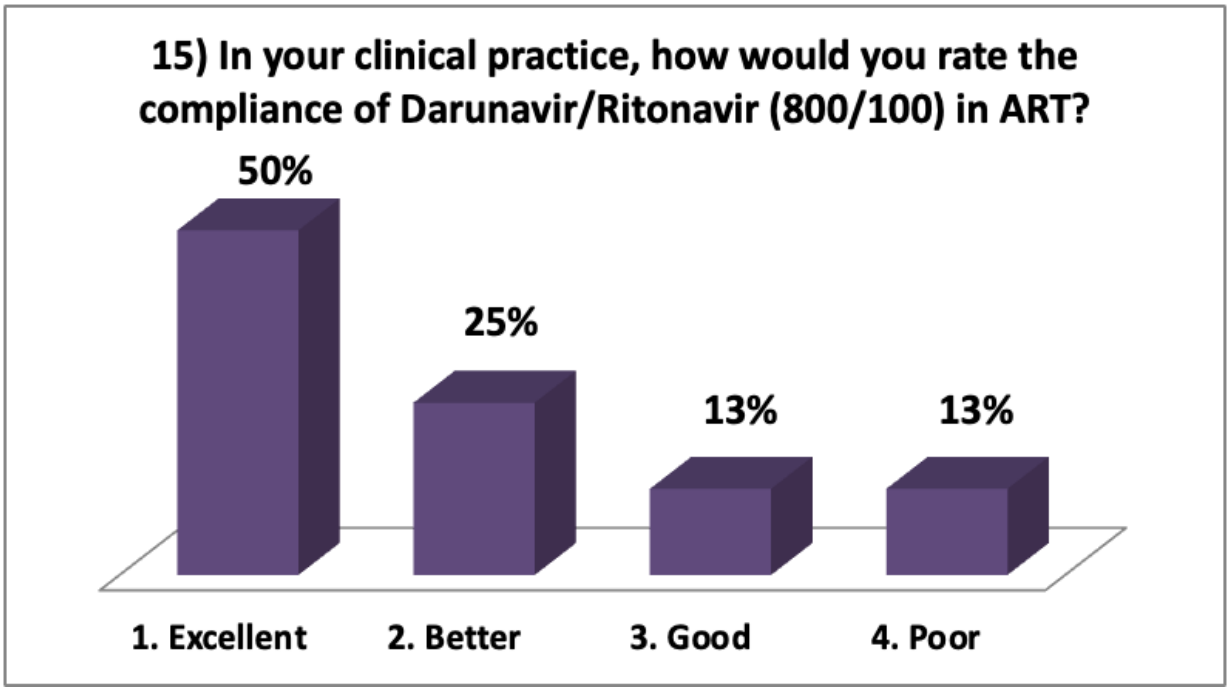
15. In your clinical practice, how would you rate the compliance of Darunavir/Ritonavir (800/100) in ART?

A. Excellent

B. Better

C. Good

D. Poor



In the clinical practice, the compliance of Darunavir/Ritonavir (800/100) in ART is rated as excellent.

SUMMARY

1. In the clinical practice, 5 to <20 patients are newly diagnosed with HIV in a month.

2. In the opinion, the incidence of HIV in Indian patients is higher in the 18-65 years age group.

3. In the clinical practice, the most common opportunistic infection presenting in patients living with HIV is TB (including pulmonary and extra-pulmonary), as reported by 50% of respondents.

4. In the clinical practice, CD4 count was monitor in patients living with HIV every 6 months.

5. In our clinical practice, the preferred boosted protease inhibitor is Lopinavir/ritonavir.

6. According to NACO, advanced HIV disease in adults, adolescents and children more than 5 years is referred to as a CD4 cell count <100 cells/mm^3.

7. According to NACO, in clinically asymptomatic individuals, for HIV testing and diagnosis in adults and children above the age of 18 months, the sample should be reactive with two different kits.

8. In the opinion, the primary benefit of prescribing fixed-dose combinations (FDCs) in ART is that they are easy for patients to take, thereby improving and promoting desirable adherence.

9. In the opinion, Lopinavir/ ritonavir has the highest genetic barrier to resistance.
10. The preferred HIV patient profile for the ART containing Darunavir/Ritonavir (800/100 mg once daily) is for the treatment of experienced patients.

11. In expert opinion, DRV/r (800/100) has potential advantages over DRV/r (600/100) in terms of fewer chances of drug resistance and better tolerability.

12. In the clinical practice, the most common adverse effect observed with Darunavir therapy is hepatotoxicity, as reported by 38% of respondents.

13. In the clinical practice, the preferred Darunavir and Ritonavir combination is once-daily Darunavir 800 mg and Ritonavir 100 mg.

14. In my opinion, the potential advantages of Ritonavir-boosted Darunavir combination include increases drug exposure and prolongs DRV half-life

15. In the clinical practice, the compliance of Darunavir/Ritonavir (800/100) in ART is rated as excellent.

CONSULTING OPINION

Market Opportunities:

The understanding of Darunavir Ritonavir (800MG and 100MG) in antiretroviral therapy (ART) presents significant market opportunities. Emerging clinical evidence supports the efficacy and safety of this combination in managing HIV infection, indicating a potential increase in demand for Darunavir Ritonavir-based regimens.

Value for Healthcare Professionals:

Healthcare professionals can derive substantial value from understanding the place of Darunavir Ritonavir in ART. This combination therapy offers a potent and well-tolerated option for managing HIV infection, particularly in treatment-experienced patients or those with resistance to other antiretroviral agents. Understanding Darunavir Ritonavir's role provides healthcare professionals with an effective tool for optimizing HIV treatment strategies, improving virological suppression, and reducing the risk of treatment failure.

Adverse Effect Management:

Effectively managing adverse effects is a crucial aspect of utilizing Darunavir Ritonavir in ART. Literature suggests that healthcare professionals should closely monitor patients for potential side effects such as gastrointestinal disturbances, hepatotoxicity, and lipid abnormalities. Establishing a robust monitoring system and patient education can aid in early detection and management of adverse effects, ensuring the safety and tolerability of Darunavir Ritonavir therapy.

Effective Management:

Darunavir Ritonavir offers effective management of HIV infection by inhibiting viral replication and reducing viral load. Healthcare professionals can leverage the potent antiretroviral activity of this combination to achieve virological suppression and improve immunological outcomes in HIV-infected individuals. Utilizing Darunavir Ritonavir-based regimens may lead to enhanced efficacy compared to other antiretroviral agents, potentially reducing the risk of virological failure and development of drug resistance.

Market Positioning:

Positioning Darunavir Ritonavir therapy in the ART market requires a strategic approach. Highlighting the efficacy, safety profile, and potential to address unmet needs in HIV management can enhance the market position of Darunavir Ritonavir-based regimens. Collaborative efforts between pharmaceutical companies, healthcare providers, and regulatory authorities are essential for successful market penetration and adoption of Darunavir Ritonavir therapy in clinical practice.

Personalized Treatment Decisions:

Understanding the place of Darunavir Ritonavir allows healthcare professionals to make personalized treatment decisions based on individual patient characteristics. Factors such as treatment history, resistance profile, and comorbidities can be considered when selecting Darunavir Ritonavir as part of an ART regimen. Personalized approaches contribute to better treatment adherence, improved virological outcomes, and overall satisfaction in HIV management.

Improving Patient Outcomes:

Utilizing Darunavir Ritonavir therapy in ART has the potential to significantly improve patient outcomes. By providing a potent and well-tolerated option for HIV treatment, Darunavir Ritonavir-based regimens may lead to better virological suppression, immunological recovery, and overall quality of life for patients living with HIV. Monitoring and optimizing therapy in collaboration with healthcare providers can contribute to sustained positive outcomes and enhanced patient well-being.

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