View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

patients. **METHODS:** A SLR identified randomised controlled trials (RCTs) of TDF/FTC or ABC/3TC plus third agents grouped by class (protease inhibitors [PI], non-nucleoside reverse transcriptase inhibitors [NNRTI] and integrase strand transfer inhibitors [INSTI]) in HIV-1 infection. MEDLINE, EMBASE and the Cochrane Library were searched in March 2014. Bayesian NMAs of RCTs in were run for virologic response (VR) and all-cause discontinuation at Week 48 (Wk48) and 96 (Wk96). Inconsistency and the effect of baseline characteristics were also assessed using unrelated mean-effects models and meta-regression, respectively. **RESULTS:** Of 1,093 citations retrieved, 243 citations were included in the SLR, reporting 18 RCTs that informed at least one network. In the NMA, fixed-effect models represented a better fit for VR data, whereas random-effects models fitted the all-cause discontinuation data best. With NNRTIs, TDF/FTC was associated with significantly higher odds of VR than ABC/3TC at Wk48 (OR 1.32 [95%CrI 1.05, 1.65]) and Wk96 (OR 1.29 [95%CrI 1.03, 1.61]). With INSTIs, TDF/FTC had a significantly higher odds of VR at Wk96 compared with ABC/3TC (OR 1.46 [95%CrI 1.04, 2.04]). No statistically significant differences in VR were found between the backbones with PIs. No statistically significant differences in all-cause discontinuation at Wk48 or Wk96 were observed between the backbones with any class of third agent. Networks showed little inconsistency, and baseline characteristics did not have any significant effect on results. **CONCLUSIONS:** TDF/FTC was associated with statistically significant VR benefits compared with ABC/3TC with NNRTIs at both Wk48 and Wk96 and with INSTIs at Wk96, and no statistically significant effect was seen with respect to all-cause discontinuation.

PIN13

META-ANALYSIS OF MORTALITY IN ADULTS, NEWBORNS AND OLDER CHILDREN WITH BACTERIAL INFECTIONS AND SEPSIS WHEN TREATED BY IGM-ENRICHED INTRAVENOUS IMMUNOGLOBULINS AND STANDARD SCHEMES

Fedyaeva VK[1], Rebrova OY[2]

[1]*The Russian Presidential Academy of National Economy and Public Administration, Moscow, Russia,* [2]*Pirogov Russian National Research Medical University, Moscow, Russia*

OBJECTIVES: There is no consistent evidence of clinical efficacy of IgM-enriched intravenous immunoglobulin (IgM) for reducing mortality in adults, newborns and older children with bacterial infections and sepsis. The aim of the study was to update evidence by considering recent clinical trials and analyzing age populations and comparators separately. **METHODS:** We searched publications in PubMed and the Cochrane Library in December 2014. All-cause mortality was analyzed, and systematic review using meta-analysis and indirect comparison was carried out. **RESULTS:** Five meta-analyses and 18 RCTs were considered, including 12 trials studied the effect of IgM in adults, 5 in newborns, and one in children 1-24 months old. All interventions were applied with basic therapy (BT). No difference between IgM and albumin was found for adults. However we found significant efficacy of IgM in adults when compared with all comparators, RR 0.69 [0.56; 0.84], and BT, RR 0.52 [0.39; 0.69]. In newborns mortality is lower in IgM than in all comparators groups, RR 0.47 [0.29; 0.76], and in BT with or without placebo, RR 0.50 [0.30; 0.84]. Children under 24 months receiving IgM also had lower mortality than in all comparators group, RR 0.48 [0.34; 0.68]. Indirect comparison of IgM and IgG in adults showed no differences, in newborns the difference is in favor of IgM, RR 0.47 [0.29; 0.77]. **CONCLUSIONS:** IgM is effective in reducing all-cause mortality in adults with bacterial infection or sepsis in comparison with BT; also in newborns in comparison with any comparators (BT with or without placebo, albumin, IgG), in children under 24 months in comparison to BT with or without albumin. Further head-to-head clinical trials are needed to enhance evidence.

PIN14

HIGH THERAPEUTIC EFFICIENCY WITH LEDIPASVIR/SOFOSBUVIR FOR THE TREATMENT OF GENOTYPE 1 CHRONIC HEPATITIS C IN PORTUGAL

Ferreira D[1], Félix J[1], Almeida J[1], Mota M[1], Afonso-Silva M[1], Silva P[1], Vandewalle B[1], Velosa J[2], Marinho R[2], Aldir I[3], Carvalho A[4], Valente C[5], Macedo G[6], Sarmento e Castro R[7], Pedroto I[8]

[1]*Exigo Consultores, Alhos Vedros, Portugal,* [2]*Hospital Santa Maria, Centro Hospitalar de Lisboa Norte, E.P.E., Lisboa, Portugal,* [3]*Hospital Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal,* [4]*Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal,* [5]*Centro Hospitalar e Universitário de Coimbra, E.P.E., Coimbra, Portugal,* [6]*Hospital de São João, Porto, Portugal,* [7]*Centro Hospitalar do Porto, E.P.E., Porto, Portugal,* [8]*Centro Hospitalar do Porto, Porto, Portugal*

OBJECTIVES: Chronic hepatitis C (CHC) is a major public health problem affecting 1.5% of the Portuguese population and reducing life expectancy by 20 years. The most recent international guidelines recommend the utilization of sofosbuvir (SOF) as backbone for the treatment of CHC patients. The association of ledipasvir (LDV) to SOF enhances SOF efficacy and safety, especially in patients infected with genotype-1 hepatitis C virus. Additionally, it allows the treatment of CHC patients without using pegylated interferon-α (PegIFN) and ribavirin (RBV). The objective of this study was to estimate LDV/SOF's contribution to the Portuguese public health by exhausting CHC therapeutic efficiency. **METHODS:** Therapeutic efficiency was defined as maximum capacity to benefit from treatment in terms of life years (LY) relative to the general population's life expectancy. The natural history of CHC and treatment implication was modelled with a Markov model allowing for long-term assessment in terms of HCV fibrosis progression. Comparators used were SOF+PegIFN+RBV, SOF+RBV, boceprevir+PegIFN+RBV and PegIFN+RBV, taking into consideration the therapeutic options currently financed by the Portuguese National Health System, the recommendation of SOF as the standard of care and the coincidence between therapeutic indications. **RESULTS:** In HCV genotype-1 non-cirrhotic patients, LDV/SOF treatment is estimated to result in 0.21 LY, 1.5 LY or 1.44-2.90 LY gained in comparison to SOF+PegIFN+RBV, SOF+RBV or the options financed by the Portuguese NHS, respectively; for patients with cirrhosis, these values are 1.20 LY, 4.08 LY or 1.33-4.67 LY, respectively. In patients infected with HCV genotype-1, LDV/SOF is expected to enhance life expectancy, with therapeutic efficiency ranging from 86.2% to 98.4%. **CONCLUSIONS:** LDV/SOF regimens are associated with high therapeutic efficiency, and are expected to maximize the years of life of the Portuguese genotype-1 HCV patients.

PIN15

MODELING OF USING RILPIVIRINE/ TENOFOVIR/ EMTRICITABINE IN TREATMENT OF NAÏVE HIV-1 INFECTED PATIENS

Yagudina R, Kulikov A, Babiy VV

I.M. Sechenov First Moscow State Medical University, Moscow, Russia

OBJECTIVES: To estimate long-term clinical outcomes of using rilpivirine/tenofovir/emtricitabine (single tablet regimen) in treatment of naïve patients with HIV-1 RNA<100 000 copies/ml in the Russian Federation. **METHODS:** The mathematical model was developed in Microsoft Office 2013. The time horizon was 5 years. The model included two submodels: Markov's model and tree-decision model. The following outcome measures were used in present study: Number of deaths, Years of life lost, Number of hospitalizations. All calculations were based on results of published clinical, epidemiological and social researches. Data for patients with HIV was obtained from prior epidemiological studies that had been provided in the Russian Federation. **RESULTS:** The number of deaths on rilpivirine/tenofovir/emtricitabine scheme (single tablet regimen) was 12% and 15% less, the number of YLL was 9% and 12% less and Number of hospitalizations was 19,91% and 19,88% less than on the schemes efavirenz + tenofovir/ emtricitabin (multi-pill regimen) and lopinavir + tenofovir/ emtricitabin (multi-pill regimen), respectively. **CONCLUSIONS:** Results obtained with present model showed that treatment naïve patients with HIV-1 RNA<100 000 copies/ml using rilpivirine/tenofovir/emtricitabine scheme (single tablet regimen) can be associated with better long-term outcomes compared to alternative multi-pill schemes.

PIN16

INDIRECT COMPARISON FOR E/C/F/TAF IN TREATMENT NAÏVE HIV PATIENTS

Leleu H[1], Rodriguez I[2], Blachier M[1], Pentel J[3]

[1]*PUBLIC HEALTH EXPERTISE, Paris, France,* [2]*Gilead, Boulogne, France,* [3]*GILEAD, Boulogne, France*

OBJECTIVES: E/C/F/TAF is the combination of Elvitegravir/Cobicistat/Emtricitabine with Tenofovir Alafenamide, a new prodrug of tenofovir with a better biodisponibility and safety profile than Tenofovir Disoproxil Fumarate (TDF) . We used adjusted indirect comparison to estimate the relative efficacy of E/C/F/TAF versus HAART based on raltegravir (RAL) or dolutegravir (DTG) in treatment-naïve HIV-1 infected patients that was not directly studied in head-to-head randomized controlled trials. **METHODS:** A systematic review of published literature was conducted to identify phase 3 randomized controlled clinical trials (up to February 2015) including at least one third agent of interest. Network adjusted indirect comparison was used to evaluate week 48 relative effectiveness (HIV-RNA suppression to 50 copies/mL) after checking for homogeneity and absence of interaction between baseline characteristics and efficacy. Analyses based on secondary networks were performed to assess validity. A ten percent margin was used for non-inferiority. **RESULTS:** Twelve studies were included in the network. Baseline patient's characteristics were slightly different between studies published before and after 2011 due to changes in 2011 in treatment initiation guidelines. No significant interactions were observed in the studies between baseline characteristics and week 48 virologic suppression. E/C/F/TAF was associated with a non-significant different rate for week 48 virologic suppression compared to DTG + ABC/3TC or RAL + TDF/FTC (Relative Risk = 0.98 (0.89 - 1.07) and 1.01 (0.92 - 1.12) respectively). Using secondary networks yielded similar results. **CONCLUSIONS:** This indirect comparison suggests that with ten percent non-inferiority margin E/C/F/TAF has a similar efficacy then DTG or RAL based HAART.

PIN17

PUBLIC HEALTH AND ECONOMIC IMPACT OF A QUADRIVALENT INFLUENZA VACCINE IN COMPARISON TO THE TRIVALENT INFLUENZA VACCINE IN BRAZIL OVER THE PERIOD OF 2010 – 2013

Bricks L[1], Lopez JG[2], Macabeo B[3], Piedade AD[4], Clark OA[4], Nishikawa AM[4], Bottoni A[4], Gonçalves T[1]

[1]*Sanofi Pasteur, São Paulo, Brazil,* [2]*Sanofi Pasteur, Mexico City, Mexico,* [3]*Sanofi Pasteur, Lyon, France,* [4]*Evidências - Kantar Health, Campinas, Brazil*

OBJECTIVES: Trivalent influenza vaccine (TIV), which contains two strains of influenza A and one strain of influenza B is recommended by the Brazilian government to prevent influenza. However, co-circulation of two distinct B lineages and difficulties in predicting which lineage will predominate in the next season led to the development of quadrivalent influenza vaccine (QIV). The aim of the study was to estimate the public health (epidemiological) and economic impact of the QIV over four influenza seasons (2010 to 2013) in the Brazilian population in comparison with TIV. **METHODS:** A static model published by Reed et al. in 2012 was adapted to Brazil and stratified by age group. The model retrospectively calculated impact using vaccine effectiveness and coverage, illness incidence, morbidity, mortality and costs related to influenza from the Public Healthcare System and Society perspectives. Vaccine effectiveness by strain and by age in the Brazilian population is not available; therefore we used vaccine effectiveness from Clements et al., which takes into account some B-lineage cross-protection. Epidemiological and resource use data were obtained from the Brazilian public system database (DATASUS) and regional studies. Costs were expressed in 2015 Brazilian Real, vaccine cost was not considered and exchange rate used was $1.00USD=3.14BRL. **RESULTS:** The use of QIV vaccination instead of TIV in the years from 2010 to 2013 would have avoided a total of additional 654,018 cases, 323,336 consultations, 7,536 hospitalizations and 1,122 deaths due to influenza. In 2013, year with high B circulation and high mismatch, considering a public payer and societal perspective, respectively, QIV vaccination could have avoided additional influenza costs estimated at BRL 11 million and 62 million (USD 3.5 million and 20 million). **CONCLUSIONS:** Vaccination with QIV for the Brazilian population is expected to result in public health benefit and less resource use when compared to TIV.