

Dr. Matt Johnson - IBD Trials Made Easy

Infliximab

- ACT 1 +2 (UC)
 - ACT 1 - Induction = 69% response at 8/52
 - ACT 2 - Maintenance = 46% at 30/52
 - Short term Mucosal healing = 53%
 - Long term Remission = 40-55% at 1 y (up to 2y)
 - Colectomy rates = Reduced from 14.8 to 9.5%
 - No increased risk of post-op complications
- ACCENT 1 (CrD)
 - Induction = 58%
 - Maintenance = 39% at 46/52
 - AB's reduced from 18% to 6% with concomitant steroids
- Swedish UC Study
 - Colectomy at 90d reduced from 67% to 29% (50% reduction in Sx)
- Leuven – Outcome in 614 Crohn's (55% Luminal, 40% Fistulae, 5% EGIMIBD)
 - Initial Response = 90% (Luminal = Fistular = EGIMIBD)
 - Sustained benefit at 5y = 63% (43% Maintenance, 20% off of IFX)
 - Mucosal healing = 58%
 - Side effects = 13% (Acute 20%, Delayed 50%, Serious 30%)
 - Dose adjustment = 19.7% (62-72% returned to standard regimen)
 - Episodic treatment = 46% had to switch to regular maintenance Rx
- Leuven – Safety
 - 734 IBD patients on IFX
 - Mortality = 1.6% (no stat diff to control group)
 - Malignancies (Lymphoma) = 2.8% (no stat diff to control group)
 - Infections = 6% (no stat diff to control group)
 - Dermatology (Psoriatic) = 20%
 - AI / Vasculitis = 0.6% (but ANA +ive in 50%)
 - Infusion Reactions = 2.3% (Acute 17%, Delayed 7%, SerumS 6%)
 - Severe adverse events = 13% (19% in none IFX control group)
 - Concomitant steroids was the greatest risk factor for infection
- SONIC
 - Steroid free remission seen in - 30% AZA, 45% IFX, 57% AZA+IFX
 - Mucosal healing seen in - 20% AZA, 30% IFX, 45% AZA+IFX

- SUTD (Step-Up Top-Down) -133
 - Mucosal healing = 30% in Step-Up Mx Vs 73% in Top-Down Mx
 - Differences were seen at 6m, but not at 1y

- REACH
 - Moderate – Severe CrD in Paediatrics
 - Week 10 - Clinical response = 88%, Clinical remission = 59%
 - Week 54 - Maintained response = 64%, Clinical remission = 56%

- GETAID
 - IFX + AZA > AZA alone
 - Steroid free remission at 12w = 75% (83% in AZA naïve) Vs 38%

- US - TREAT Registry > 6,000
 - Mortality of patients on IFX = off IFX
 - No increased risk of mortality, malignancy, lymphoma or infection
 - 2x Infection risk with concomitant steroids
 - 6x Infection risk with concomitant Narcotics
 - 9x Infection risk with concomitant Narcotics + IFX
 - 10x Infection risk with concomitant Narcotics + Steroids
 - 3.3% infusion reactions
 - 0.08% serious infusion reactions

- European ENCORE CD
 - Concomitant steroids = major independent risk factor for infection

- STORI
 - 60% of CrD patients remain in remission 1 y after stopping IFX provided mucosal healing has been achieved

- Siegel C.A 2008
 - Lymphoma in CrD = 0.02%
 - Lymphoma on Immunologicals = 0.04%
 - Lymphoma on Biologicals = 0.06%

Adalimumab

•CLASSIC I + II

- CLASSIC 1 - 150 naïve patients = Clinical response 59% (Placebo 37%)
- = Remission 36% (Placebo 12%)
- = Induction at 160 > 80mg
- CLASSIC 2 - 55 in remission = Maintenance@1y 79% (Placebo 44%)

•GAIN

- Remission achieved in 22% who had failed on IFX
- Induction at 160mg > 80mg
- 325 IFX Intolerant patients = Clinical response 52% (Placebo 34%)
- = Remission 21% (Placebo 7%)

•CHARM

- 499 Responders of ADA = Maintenance 36% (Placebo 12%)
- Shorter disease duration do better

•SWITCH

- 73 patients stabilized on IFX, 37 continue on maintenance, 36 were switched to ADA with an initial loading dose of 80mg, then 40mg e2w
- 38.9% required dose increases (Vs 14% on IFX)
- trial terminated early as 22% on ADA required rescuing with IFX

•EXTEND

- Mucosal healing at 3/12 predicts outcome at 1 year.
- Better outcome with initiation from 160mg (40%)
- Early mucosal healing 33x more likely remission @ 1y

•ADHERE

Other Important IBD Papers

- Eaden JA 2001 GUT
 - Cancer risk in UC = 2% at 10y, 8% at 20y, 18% at 30y
- Langholz E 1994 Gastro – 1161 Denmark
 - Colectomy risks in UC = 20% at 10y, 30% at 25y
- Cosnes J 2002 IBD – 2000 CrD
 - Stricturing Complications = 12.7%
 - Penetrating Complications = 47%
- Rubin DT 2007 Gastro
 - Colectomy risk doubles per 1 point increase in AHS (total out of 6)
- Gupta RB 2007 Gastro
 - Cancer risk triples per 1 point increase in AHS (total out of 6)
- Maser EA 2006 Clin GH
 - Detectable IFX Trough Levels pre-infusion significantly increases
 - Clinical remission rate = 82% Vs 6% (Detect Vs Undetect)
 - Endoscopic improvement at 52w = 88% Vs 33%