**Table S3.** Procedures grouped by risk category as described by Afdhal et al. 2012. Percentages reported as event rate/total patients.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Risk | Procedure | Placebo | TPO-RA | No. studies |
| All | Total number of procedures / no. patients | 474 / 512 pts | 691 / 717 | 6 |
| 1 | Risk Category 1 procedures - no. (% all procedures) | 294 (62.00%) | 404 (58.48%) |  |
| **Paracentesis** | 5 | 10 | 4 |
| **All endoscopic procedures** | 175 | 260 |  |
| Esophagogastroduodenoscopy (EGD) | 162 | 236 |  |
| *Therapeutic EGD\** | 90 | 140 | 3 |
| *Diagnostic EGD* | 60 | 74 | 2 |
| *EGD NOS* | 12 | 22 | 2 |
| Colonoscopy | 9 | 22 |  |
| *Colonoscopy with polypectomy* | 8 | 10 | 1 |
| *Colonoscopy without biopsy/polypectomy* | 1 | 12 | 1 |
| Argon plasma coagulation (APC) | 4 | 2 | 1 |
| **All HEENT procedures** | 31 | 44 | 1 |
| *Dental procedure* | 29 | 43 | 4 |
| *Non-dental HEENT procedure* | 2 | 1 | 1 |
| Gastrointestinal endoscopic procedures, large-volume paracentesis, dental extractions ^ | 83 | 90 | *Afdhal* |
| 2 | Risk Category 2 procedures - no. (% all procedures) | 85 (17.95%) | 143 (20.69%) |  |
| **Liver procedure** | 64 | 117 |  |
| RFA | 44 | 95 | 4 |
| Liver biopsy | 16 | 17 | 6 |
| Other liver procedure | 4 | 2 | 1 |
| Percutaneous ethanol injection therapy | 0 | 3 | 2 |
| **Laparoscopic procedures** | 1 | 3 |  |
| Inguinal hernia repair | 1 | 1 | 1 |
| Umbilical hernia repair | 0 | 1 | 1 |
| Other laparoscopic procedure | 0 | 1 | 1 |
| Percutaneous needle biopsy of an organ, primary HCC resection/ablation, laparoscopic procedures ^ | 20 | 23 | *Afdhal* |
| 3 | Risk Category 3 procedures - no. (% all procedures) | 72 (15.20%) | 78 (11.28%) |  |
| **Vascular procedure** | 72 | 78 |  |
| *Transarterial chemoembolization* | 43 | 53 | 3 |
| *Transjugular intrahepatic portosystemic shunt* | 3 | 0 | 1 |
| *Vascular catheterization* | 26 | 25 | 2 |
| 4 | Risk Category 4 procedures - no. (% all procedures) | 4 (0.84%) | 4 (0.58%) |  |
| **Open incision of body cavity or tissue space ^** | 4 | 4 | *Afdhal* |
| Unk. | Unknown risk category procedures - no. (% all procedures) | 19 (4.01%) | 62 (8.97%) |  |
| **Other non-invasive procedures** | 2 | 2 |  |
| *Diagnostic thoracentesis* | 1 | 0 | 1 |
| *Cystoscopy and biopsy of urinary bladder* | 1 | 0 | 1 |
| *Removal of cervical polyp* | 0 | 1 | 1 |
| *Bone marrow biopsy* | 0 | 1 | 1 |
| Other | 17 | 60 | 2 |
| NA | No procedure | 30 | 20 | 3 |

*\* = variceal ligation, banding, sclerotherapy and/or biopsy Unk. = unknown; HEENT = head ear eyes nose throat*

*^Afdhal 2012 published number of procedures in TPO-mimetic and placebo in summary based on the above risk categories. Procedures are thus presented in groupings for Afdhal participants.*

**Table S4.** Safety endpoints of bleeding and thrombosis events, reported as event rate.

|  |  |  |  |
| --- | --- | --- | --- |
| Bleeding event | Placebo (events) | Tpo-RA (events) | No. studies |
| Total (events/patients) | 80/512 (15.6%) | 83/717 (11.6%) | 8 |
| Anemia\* | 1 | 10 | 3 |
| Contusion | 6 | 6 |  |
| *Contusion* | *6* | *2* | *5* |
| *Ecchymoses* | *0* | *3* | *2* |
| *Post-procedural contusion* | *0* | *1* | *1* |
| Hematoma | 8 | 3 |  |
| *Eyelid hematoma* | *1* | *0* | *1* |
| *Hematoma* | *5* | *2* | *3* |
| *Post-procedural hematoma* | *1* | *1* | *1* |
| *Tongue hematoma* | *1* | *0* | *1* |
| Subcutaneous bleeding | 7 | 9 |  |
| *Ear hemorrhage* | *1* | *0* | *1* |
| *Petechiae* | *5* | *2* | *4* |
| *Purpura* | *0* | *3* | *2* |
| *Subcutaneous hemorrhage*  | *1* | *4* | *2* |
| Hematuria | 10 | 2 | 3 |
| Mucosal bleeding (non-GI) | 24 | 11 |  |
| *Conjunctival hemorrhage* | *2* | *0* | *1* |
| *Epistaxis* | *14* | *9* | *6* |
| *Gingival bleeding* | *6* | *0* | *3* |
| *Hemoptysis* | *1* | *2* | *2* |
| *Pharyngeal hemorrhage* | *1* | *0* | *1* |
| Gastrointestinal bleeding | 9 | 23 |  |
| *Esophageal hemorrhage*  | *0* | *2* | *2* |
| *Esophageal variceal hemorrhage* | *3* | *0* | *3* |
| *Gastric hemorrhage* | *1* | *4* | *3* |
| *GI hemorrhage NOS* | *1* | *1* | *2* |
| *Hematemesis* | *0* | *2* | *2* |
| *Hematochezia* | *1* | *3* | *2* |
| *Rectal hemorrhage* | *3* | *5* | *3* |
| *Upper GI hemorrhage* | *0* | *6* | *4* |
| Hemorrhage NOS | 15 | 19 |  |
| *Incision site hemorrhage* | *1* | *3* | *2* |
| *Injection site hemorrhage* | *2* | *0* | *1* |
| *Post-procedural hemorrhage* | *4* | *9* | *4* |
| *Procedural hemorrhage* | *3* | *6* | *3* |
| *Puncture site hemorrhage* | *3* | *0* | *1* |
| *Retinal hemorrhage*  | *1* | *0* | *1* |
| *Splenic hemorrhage* | *0* | *1* | *1* |
| *Traumatic hemorrhage* | *1* | *0* | *1* |
| **Thrombotic events** | **Placebo** | **Tpo-RA** | **No. studies** |
| Total (events/patients) | 9/512 (1.8%) | 16/717 (2.2%) | 8 |
| Studies without PVT screening | 3/163 | 7/196 | 4 |
| Studies with PVT screening | 6/246 | 8/330 | 2 |
| Studies with no thromboses | 0/103 | 0/191 | 2 |

*\* No uniform threshold referenced by studies with anemia as bleeding outcome.*

*Unable to estimate severity of bleeding episodes given lack of uniformly adopted bleeding severity score.*