**Supplementary Table 2. Updated RUCAM for the hepatocellular injury of DILI and HILI**

| **Items for Hepatocellular Injury** | **Score** | **Result** |
| --- | --- | --- |
| 1. Time to onset from the beginning of the drug/herb |  |  |
| ●   5–90 days (rechallenge: 1–15 days) | +2 | □ |
| ●   <5 or > 90 days (rechallenge: > 15 days) | +1 | □ |
| Alternative: Time to onset from cessation of the drug/herb |  |  |
| ●   ≤ 15 days (except for slowly metabolized chemicals: > 15 days) | +1 | □ |
| 2. Course of ALT after cessation of the drug/herb |  |  |
| Percentage difference between ALT peak and N |  |  |
| ●   Decrease ≥ 50% within 8 days | +3 | □ |
| ●   Decrease ≥ 50% within 30 days | +2 | □ |
| ●   No information or continued drug use | 0 | □ |
| ●   Decrease ≥ 50% after the 30th day | 0 | □ |
| ●   Decrease < 50% after the 30th day or recurrent increase | −2 | □ |
| 3. Risk factors |  |  |
| ●   Alcohol use (current drinks/d: > 2 for women, > 3 for men) | +1 | □ |
| ●   Alcohol use (current drinks/d: ≤ 2 for women, ≤ 3 for men) | 0 | □ |
| ●   Age ≥ 55 years | +1 | □ |
| ●   Age < 55 years | 0 | □ |
| 4. Concomitant drug(s)/herb(s) |  |  |
| ●   None or no information | 0 | □ |
| ●   Concomitant drug/herb with incompatible time to onset | 0 | □ |
| ●   Concomitant drug/herb with compatible or suggestive time to onset | −1 | □ |
| ●   Concomitant drug/herb known as hepatotoxin and with compatible or suggestive time to onset delete marking right side above | −2 | □ |
| ●   Concomitant drug/herb with evidence for its role in this case (positive rechallenge or validated test) | −3 | □ |
| 5. Search for alternative causes | Tick if negative | Tick if not done |
| Group I (7 causes) |  |  |
| ●   HAV: Anti-HAV-IgM | □ | □ |
| ●   Hepatobiliary sonography / color Doppler | □ | □ |
| ●   HCV: Anti-HCV, HCV-RNA | □ | □ |
| ●   HEV: Anti-HEV-IgM, anti-HEV-IgG, HEV-RNA | □ | □ |
| ●   Hepatobiliary sonography/color Doppler sonography of liver vessels/ endosonographic/CT/MRC | □ | □ |
| ●   Alcoholism (AST/ALT ≥ 2) | □ | □ |
| ●   Acute recent hypotension history (particularly if underlying heart disease) | □ | □ |
| Group II (5 causes) |  |  |
| ●   Complications of underlying disease(s) such as sepsis, metastatic malignancy, autoimmune hepatitis, chronic hepatitis B or C, primary biliary cholangitis, or sclerosing cholangitis, genetic liver diseases | □ | □ |
| ●   Infection suggested by PCR and titer change for |  |  |
|   ●  CMV (anti-CMV-IgM, anti-CMV-IgG) | □ | □ |
|   ●  EBV (anti-EBV-IgM, anti-EBV-IgG) | □ | □ |
|   ●  HSV (anti-HSV-IgM, anti-HSV-IgG) | □ | □ |
|   ●  VZV (anti-VZV-IgM, anti-VZV-IgG) | □ | □ |
| Evaluation of groups I and II |  |  |
| ●   All causes-groups I and II—reasonably ruled out | +2 | □ |
| ●   The seven causes of group I ruled out | +1 | □ |
| ●   6 or 5 causes of group I ruled out | 0 | □ |
| ●   Less than five causes of group I ruled out | -2 | □ |
| ●   Alternative cause highly probable | -3 | □ |
| 6. Previous hepatotoxicity of the drug/herb |  |  |
| ●   Reaction labeled in the product characteristics | +2 | □ |
| ●   Reaction published but unlabeled | +1 | □ |
| ●   Reaction unknown | 0 | □ |
| 7. Response to unintentional re-exposure |  |  |
| ●   Doubling of ALT with the drug/herb alone, provided ALT below 5 N before re-exposure | +3 | □ |
| ●   Doubling of ALT with the drug(s)/herb(s) already given at the time of first reaction | +1 | □ |
| ●   Increase of ALT but less than N in the same conditions as for the first administration | −2 | □ |
| ●   Other situations | 0 | □ |
| Total score for the case | □ |

The items specifically refer to the hepatocellular injury rather than to the cholestatic or mixed liver injury.1

Total score and resulting causality grading: ≤ 0, excluded; 1–2, unlikely; 3–5, possible; 6–8, probable; ≥ 9, highly probable. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CMV, cytomegalovirus; CT, computed tomography; DILI, drug-induced liver injury; EBV, Epstein-Barr virus; HAV, hepatitis A virus; HBc, hepatitis B core; HBsAg, hepatitis B antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus; HILI, herb-induced liver injury; HSV, herpes simplex virus; MRC, magnetic resonance cholangiography; N, upper limit of the normal range; RUCAM, Roussel Uclaf Causality Assessment Method; VZV, varicella zoster virus.

**Reference**

1. Danan G, Teschke R. RUCAM in drug and herb induced liver injury: the update. Int J Mol Sci 2015;17(1):14. doi: 10.3390/ijms17010014, PMID: 26712744