An innovative germline DNA test which predicts genetic susceptibility to severe 5FU/capecitabine toxicity

ToxNav workflow steps 1–7:

1. Patients offered fluoropyrimidine chemotherapy
   - ToxNav test requested by clinician

2. Blood sample taken (EDTA)
   - Sample requisition form and blood sample sent to laboratory

3. Sample and requisition form received and logged by laboratory
   - DNA extracted

4. Sequencing carried out to detect genotype of 19 variants
   - Data managed via secure server

5. Results transmitted from lab to OCB analysis suite
   - Data imported to ToxNav software

6. **Phenotype (genotype)** | **ToxNav Risk Category** | **Implications for Phenotypic Measures** | **Dosing Recommendations** (not patients with the other contraindicating factors)
---|---|---|---
DPYD normal metabolizer | Standard Risk | Normal DPYD activity and normal risk of toxicity | No indication to change dose or therapy
| Standard Risk High Risk HFS | Normal DPYD activity and normal risk of toxicity. High risk of Hand-Foot Syndrome (HFS) | No indication to change dose or therapy Prevent HFS according to local guidelines
DPYD intermediate metabolizer | High Risk | Decreased DPYD activity and increased risk of severe or fatal toxicity | A capecitabine or 5FU monotherapy dose reduction of 50% is recommended
DPYD poor metabolizer | Critical Risk | Complete DPYD deficiency and increased risk for severe or fatal toxicity | Capecitabine or 5FU therapy is contraindicated and should not be administered

7. ToxNav report is received by the clinician within ten working days of sample receipt
   - The toxicity risk is discussed with the patient and a personalised treatment decision is made
What is ToxNav?

- A comprehensive panel of 19 genetic variants associated with 5FU/capecitabine toxicity in the DPYD and TYMS/ENOSF1 genes
  - Includes variants not found in other panels:
    - Variants found at a relatively low population frequency linked to severe (Grade 4) toxicities that may have fatal consequences
    - Hand Foot Syndrome
  - Uses the proprietary ToxNav algorithm to determine patient risk category
  - Panel derived from meta-analysis of all published genes associated with 5FU toxicity (n=4,855)

- Developed using QUASAR 2 clinical trial samples and data set
  - Well-documented toxic effects using CTCAE classifications

What does ToxNav do?

- Stratifies patients into risk groups based on their individual genotype
- 100% specificity for identification of people likely to die from 5FU/capecitabine toxicity
- Identifies risk of Grade 4 haematological toxicities with a high degree of accuracy (98% specificity, 75% sensitivity, NPV 1, PPV 0.14)

Why use ToxNav?

- Comprehensive panel of genetic variants providing optimum detection in general population
- Clinical validation in 888 colorectal patient samples from a large scale clinical trial
- Could save 10 in every 1,000 patients tested
- Potential savings of >£2,500 per patient who avoids Grade 3+ toxicities
- Meets patient safety and enhanced patient experience standards (NHS Outcomes Framework)