Whole genome sequencing (WGS) can classify diagnostically challenging tumors (1133P)

L.J. Schipper1; P. Snaebjornsson2; K.G. Samsom3; L.J.W. Bosch4; F. Lalezarif; P. Priestley5; C. Shale6; A.J. van den Broek6; N. Jacobs6; P. Roopeeman7; J.J.M. van der Hoeven7; N. Steeghs5; E. Cuppen2; G.A. Meijer1; E.E. Voest1; K. Monkhorst1

1,2,5,6 The Netherlands Cancer Institute, 3 Department of Molecular Oncology, 4Pathology, 5Radiology, and 6Medical Oncology, 4, Hartwig Medical Foundation Australia, 1Hartwig Medical Foundation

Background

- Cancer of unknown primary (CUP) remains an ongoing clinical challenge
- Genomic characterization can be used for tumor type prediction
- A WGS-based tumor type ‘cancer of unknown primary prediction algorithm’ (CUPPA) was developed, validated, and applied to 47 patients with a diagnostically challenging tumor

Methods

- CUPPA combines three DNA classifiers into an overall prediction (fig. 1)1-4.5
- Predictive performance of CUPPA was analyzed in a validation cohort of samples with known tumor origin (n=451)
- CUPPA was applied to 23 patients with a CUP and 24 patients with an inconclusive diagnosis

Predictive performance of CUPPA (validation cohort)

- Correct classification in 380/463 samples of known origin (tab. 1)
- High predictive accuracy across majority of tumor types (fig. 2)
- Simplicity likelihood score can be used to increase prediction confidence (fig. 3)

Clinical utility of CUPPA

- A high-confidence prediction was reached for 10/23 CUP patients

In 4/13 low-confidence predictions, expert pathologist(s) indicated the prediction to be informative within the clinicopathological context to narrow differential diagnosis

In 24 patients with an inconclusive final diagnosis, a high-confidence prediction alleviated diagnostic uncertainty in 17 patients (data not shown). In total, WGS/CUPPA provided diagnostic insights in 31/47 patients with a diagnostically challenging tumor (fig. 5)

Conclusions

- CUPPA can classify 75% of tumors of known origin with 95% predictive accuracy based on a high-confidence prediction
- When applied to CUP patients, a high-confidence prediction provided a probable diagnosis in 10/23 patients. Low-confidence predictions could be used to guide differential diagnoses in 4/13 CUP patients
- Diagnostic uncertainty could be alleviated in 17/24 inconclusive cases
- CUPPA algorithm can assist clinical decision making in diagnostically complex tumors

Correspondence to: k.monkhorst@lki.nl; no conflicts of interest to declare