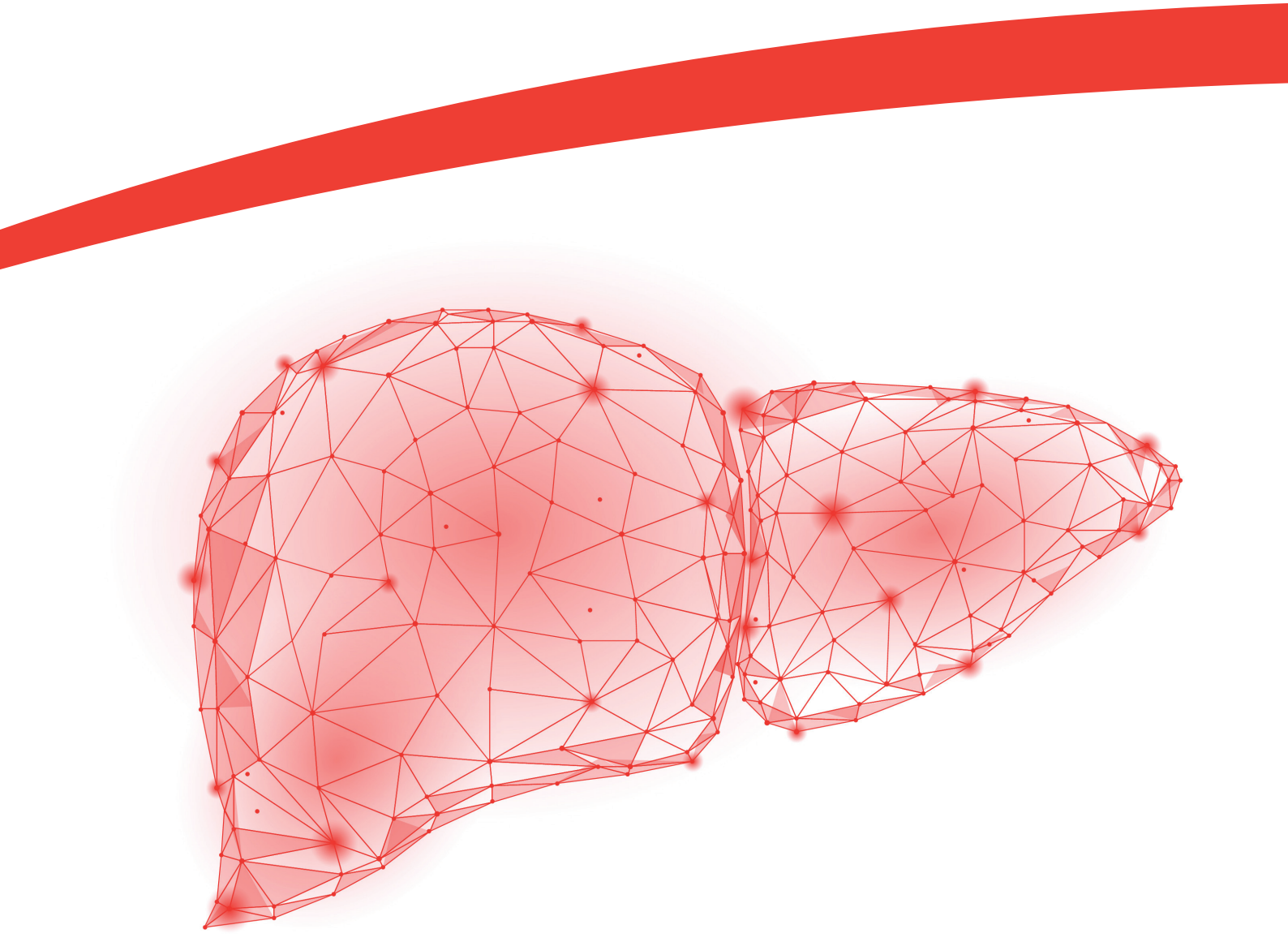
ALMAC

Partnering to Advance Human Health

PNPLA3 Genotyping Clinical Trial Assay

Determine molecular eligibility for MASH/MASLD trials



PNPLA3 Assay Specification

Intended Use

The PNPLA3 Genotyping Clinical Trial Assay (CTA) is a qualitative polymerase chain reaction (PCR) in vitro diagnostic (IVD) assay that allows identification of the I148M (rs738409) genotype within the PNPLA3 gene from DNA isolated from whole blood or buccal swabs and using the QuantStudio5™ Dx instrument.

The Assay will be used to determine the PNPLA3 genotype of subjects that are candidates for clinical trials, evaluating the clinical safety and effectiveness of investigational medicinal products for the treatment of MASH/MASLD.

The PNPLA3 Genotyping CTA is intended for investigational use only, with testing to be performed at Almac Diagnostic Services' Clinical Laboratory Improvement Amendments (CLIA) / College of American Pathologists (CAP) accredited laboratories located at 19 Seagoe Industrial Estate, Craigavon, BT63 5QD, UK and 4238 Technology Drive, Durham, NC, USA.

Assay Overview

Almac Diagnostic Services has developed the PNPLA3 Genotyping CTA for the Intended Use described above. The PNPLA3 Genotyping CTA is a qualitative IVD assay that uses PCR for allelic discrimination of rs738409 (C>G) within the PNPLA3 gene from DNA derived from whole blood or buccal swab specimens. DNA is extracted using the Qiagen® QIAamp DSP DNA Blood Mini kit and QIAamp DNA Mini kit respectively, and PCR is performed on the QuantStudio5™ Dx instrument.

The assay is designed to process up to 22 specimens per run with a turnaround time of 5-7 days from specimen receipt at Almac Diagnostic Services.

Assay Summary

Performance Specifications			
Parameter	Point Estimate	Lower 95% CI	Upper 95% CI
Analytical Precision (Craigavon): Repeatability Reproducibility	 100% 100%	 N/A 96.57%	 N/A 100.00%
Analytical Precision (Durham): Repeatability Reproducibility	 100% 100%	 N/A 96.47%	 N/A 100.00%
Analytical Specificity	N/A	N/A	N/A
Analytical Sensitivity (LoD)	N/A	N/A	N/A
Analytical Accuracy			
OPA (Craigavon and Durham)	100%	96.30%	100.00%
Sensitivity (Wildtype Allele)	100%	96.07%	100.00%
Specificity (Wildtype Allele)	100%	60.97%	100.00%
Sensitivity (Alternative Allele)	100%	92.59%	100.00%
Specificity (Alternative Allele)	100%	93.12%	100.00%

Parameter	Point Estimate	Lower 95% CI	Upper 95% CI
Interference Studies			
OPA (Blood)	100%	72.25%	100.00%
Wildtype Allele PPA (Blood)	100%	67.56%	100.00%
Wildtype Allele NPA (Blood)	100%	34.24%	100.00%
Alternative Allele PPA (Blood)	100%	60.97%	100.00%
Alternative Allele NPA (Blood)	100%	51.01%	100.00%
OPA (Buccal)	100%	72.75%	100.00%
Wildtype Allele PPA (Buccal)	100%	67.56%	100.00%
Wildtype Allele NPA (Buccal)	100%	34.24%	100.00%
Alternative Allele PPA (Buccal)	100%	60.97%	100.00%
Alternative Allele NPA (Buccal)	100%	51.01%	100.00%
Reportable Range	N/A	N/A	N/A
Reference Interval	N/A	N/A	N/A
Linearity	N/A	N/A	N/A

Assay Controls

QC steps have been established for all critical stages of the assay from specimen receipt through to genotype calling and include the following end to end process controls:

- Negative Process Control (rs738409 **homozygous** C/C)
- Positive Process Control (rs738409 **homozygous** G/G)
- Positive Process Control (rs738409 **heterozygous** C/G)

Specimen Criteria

The assay is designed to be **compatible with 20ng of DNA derived from one of the following specimen types:**

- **Whole Blood** *(collected in PAXgene Blood DNA tubes or K2 or K3 EDTA Blood collection tubes)*
- **Buccal Swab** *(collected in Mawi iSWAB-Discovery Buccal tubes)*

Level of Analytical Validation & Compliance

Analytical Validation

- CLIA/CAP
- CLEP
- CE-IVD (for use in clinical trials)

Compliance

- 21 CFR 820.30
- 21 CFR 812
- ISO 13485
- ISO 14971
- IEC 62304
- 21 CFR Part 11
- EU and US Regulation Compliant for Clinical Trial Use

Critical Reagents, Equipment & Software

Critical reagents, equipment and software required for the assay, along with validation details and a comprehensive description of the assay process flow can be provided upon request.

Contact Us

Contact your Almac Business Development Representative for more information on the Almac PNPLA3 assay.

You can also visit our website and get in touch at:

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