illumına®

BaseSpace Variant Interpreter Release Notes

BaseSpace Variant Interpreter v2.4.1

February 2018

INTRODUCTION

These Release Notes detail new features, known issues, and recently resolved issues for the BaseSpace Variant Interpreter software. For details on how to operate BaseSpace Variant Interpreter software, see the online help, which is available from the Help icon in the application.

Software Release Build:
- BaseSpace Variant Interpreter: v2.4.1.2363
- BaseSpace Knowledge Network: v1.2.24
- Case Log: v38-e23a7d0
- Nirvana: v1.6.2
- Track-level Genome Browser (AWS-US): v1.0.45
- Track-level Genome Browser (AWS-EU): v1.0.47
- Integration Service: v2.4.0
- Ontology Service: v1.2.0, build #947d107
- Static visualization: v1.0.26
- Workgroup administration console: v1.1.16, build #g0c86ae3

NEW FEATURES

Data Import and Case Setup
- Manifest
  - Tumor type can now be added as an HPO or SNOMED identifier (format – HP:XXXXXX or NNNNNN) under the Tumor Type column of the manifest file for somatic cancer cases. The identifier is used to display On/Off tumor associations on the variant grid.
  - Improved management of manifest data.
- The Sex for tumor samples can now be set to Unknown.

Case Management
- Case Registry Grid
  - The grid includes new columns for Created Date (the date the case was loaded) and Last Updated Date (last date on which the case was reanalyzed). Columns are sortable to display the latest loaded or updated cases.
  - The Status column now includes an option to toggle display of cases by status.
  - Closed cases are now hidden by default.

Case View
- Unified Variant Grid
  - Variant grid now supports review and filtering of SNVs, MNVs, Indels, CNVs, and SVs within a single variant grid tab and filter configurations.
  - Variant column sort behavior remains agnostic of variant type and sorts by genomic position.
  - Consequence column sort behavior groups variants by SVs, CNVs, and small variants (SNVs, MNVs, and Indels), then by transcript consequence for small variants and SVs or number of copies for CNVs.
  - Genes in the variant grid link to OMIM gene content.
- New Filters
  - Variant filters now support filtering variants by case-specific attributes such as variant flag, interpretation, or report inclusion.
  - Filters can now be saved from within the filtering dialog.

- o Filtering by OMIM gene is enabled.
- Variant Review
  - o Genome Viewer (IGV) now displays amino acid translations of the DNA sequence as an additional track.
  - o Coverage values for genes and exons imported from the WGS app in BaseSpace Sequence Hub can now be viewed and explored.
- Zygosity Support for CNV and SV
  - o In germline cases, zygosities are now shown and filterable for CNV and SV variants.
  - o Small variants overlapping a CNV loss event undergo an additional genotype and zygosity correction to reflect missing copies. Corrected values are shown along with the original genotype and zygosity values; both corrected and uncorrected values are filterable attributes.
- Case-level Visualizations
  - o Mutational Signature Plot
    - ▪ Mutational signature plots are now disabled for tumor-only cases to provide more accurate predictions; mutational signatures were trained on tumor-normal samples.
- Somatic Cancer Cases: Family Information
  - o In somatic cancer cases, the family information section is no longer shown on the analysis results metadata page.
- Nirvana content source versions and last updated dates are now provided on the case view and PDF report.

BaseSpace Knowledge Network (Variant Curation Portal)

- Association Page
  - o You must be logged in to the BaseSpace Knowledge Network to access private workgroup data. To prevent unauthorized user access, you are automatically logged out after a period of inactivity.
- Bulk Upload
  - o Bulk upload is now supported on the Upload Log page. View previously uploaded files, link to created associations, and investigate issues in a bulk upload. Templates are available per association type to provide an entire list of required and optional fields.
  - o HGVS nomenclature standards format (v15.11) is implemented to ensure all amino acid and codon level associations adhere to these recommendations.
- Exon-, Codon-, and Amino Acid-level curations
  - o Exon, Codon and Amino Acid associations can be added from the Add Curation dialog. The association details are displayed Variant Details page during a case review.
- Import from shared workgroups
  - o You can now import associations from a shared workgroup into their private knowledgebase. Supported association types include Mendelian, Predictive, Prognostic, Molecular Classification, and Clinical Trials.

Case-level Variant Classification & Interpretation

- Selected Associations
  - o A variant can be specified as the primary association, which automatically includes the variant in the report.
  - o At the case level, you can use primary associations to evaluate multiple associations and select the ones most relevant to be included on the final report.

- o Variants are categorized based on the severity for a given phenotype. Associations derived from the BSKN workgroup include publications and curation summary in the PDF reports.
- Variant Details – Display of KnowledgeBase and Knowledge Network information
  - o The association category (Clinical trial, Mendelian etc.) is no longer shown minimized.
  - o Open and Close dates are shown for Clinical trials in the minimized view.
  - o Assembly information on which the association was added has now been moved from the minimized view to the association details section.

Report Generation and Data Export

- Variant Grid Export
  - o SNV/Indel exports now include alt allele depth, total read depth, variant read frequency, and custom annotations.
  - o SV variant exports now include paired read support and split read support.
- Nirvana content source versions or last updated dates are now provided on the case view and PDF report.
- For rare disease cases, Contribution to Phenotypes and Inheritance Mode is only supported for SNVs in the report.
- Validation status and method are now carried forward into the report

Miscellaneous

- System-wide User Notification
  - o Variant Interpreter can now display system-wide notifications to provide announcements to users.

RESOLVED ISSUES

Issue Key	Issue Category	Description
ICL-600	API Results	API now returns the correct allelic counts for ref.
ICL-719	API Results	Allele counts are now correct for sex chromosomes.
ICL-723	API Results	PAR regions for GRCh38 are now supported.
ON-5391	Associations	Associations can now be created with multiple biomarkers of different mutation class.
ON-5713	Associations	After the "Assign" action, the date of the association is now properly updated.
BSVI-27640	Case Metadata	Selecting a sibling's sex when adding a sibling as an associated analysis on the case page is now correctly saved to the case.
BSVI-31365	Case Metadata	In Trio analysis, coverage data now correctly shows data for each family member.
BSVI-30341	Data Export	Somatic data export for CNV and SV variants does not include empty fields GQX and quality fields in export.
BSVI-30504	Filters	When applying filters, the filter summary might not list selected filter. To view a list of all applied filters, apply the filter or view in the case grid.
ICL-739	Needle Plot	Needle Plot now displays the correct visual range for all genes.

Issue Key	Issue Category	Description
ICL-740	Needle Plot	APIs for "Needle Plot" and "Variant IDs" now returns the correct number of results.
BSVI-30037	Validation Status	Technical validation of variants are now supported and are included in the report.
BSVI-28269	Workgroups	Added restrictions on workgroup access after administrator-based user removal from a workgroup.

KNOWN ISSUES

Issue Key	Issue Category	Description
ICL-837	Allele Frequency	Newly ingested samples with missing chromosomes other than chrY may contribute incorrectly to total sample counts and incorrect allele frequency.
BSVI-30507	Audit Log	Date selection is not inclusive of the selected dates, which is unintuitive. For example, to select a log for 01/15/2018, select dates from 01/14/2018 to 01/16/2018.
BSVI-26788	Bulk Actions	Bulk actions do not function properly in IE11.
BSVI-31340	Bulk Actions	Bulk actions drop-down does not display properly in Safari 10.0.1.
BSVI-32414	Bulk Actions	Application of a second bulk filter on Case Registry page overwrites a first bulk filter instead of opening a new tab.
BSVI-30305	Case Metadata	Contribution to Phenotypes and Inheritance Mode is missing from germline report for SVs and CNVs.
BSVI-29665	Case Registry	Pagination breaks if all cases are in Action Required status.
BSVI-32574 and BSVI-32671	Curation	New codon-level curations created in BaseSpace Knowledge Network do not appear in BSVI.
ON-6173	Curation	The codon count is not updated when a codon-level curation is saved successfully.
BSVI-32573	Filtering	OMIM filtering occasionally returns variants with no apparent OMIM gene.
BSVI-32600	Genome Browser	Reads with aberrant quality are marked by a colored frame that is incomplete when there is a gap in alignment.
BSVI-31659	Logging	Variant comments currently do not appear in the audit log.
ICL-721	Needle Plot	Variants with multiple consequences are returned only once with the needle plot data.
ICL-724	Needle Plot	Some variants are missing from the Variant Index that do occur in the Gene Index.
ICL-847	PheWAS	Samples can get counted multiple times when computing allele counts from samples stratified by phenotypes or other clinical attributes.

Issue Key	Issue Category	Description
BSVI-18663	Settings	The original files for Custom annotations and Gene and Region Lists that were uploaded prior during the Beta period cannot be downloaded.
BSVI-30309	Variant Associations	Updating an association foes not automatically dissociate it from existing interpretations.
BSVI-27730	Variant Details	Some variants that do not overlap known genes are nonetheless associated with gene associations.
BSVI-27938	Variant Details	In Germline cases, past cases do not show up if the variant is not mapped to a known gene.
BSVI-30418	Variant Details	Higher order associations for a case cannot be submitted.
BSVI-32324	Variant Details	Association for variants cannot be added without transcript information.

FEATURE REQUEST UPDATES & ISSUE CLARIFICATIONS

Issue Key	Issue Category	Description
BSVI-24043	Case Management	Case status and owner can be edited via the status dropdown. However, data processing statuses (Action Required, Failed, etc.) are still be displayed on the Case Registry page. See help for more information.
ON-636	Curation Portal	API should return an appropriate error message when a given parameter value does not exist. This issue does not affect the end user of the software
ON-639	Curation Portal	Gene autocomplete API has inconsistent sorting behavior for returned lists of matching genes. For the user, ordering of terms is not sorted, but does not impact results.
ON-432	Gene list manager	Expansion to related phenotypes sometimes yields results that are too distant.

When performing phenotype search, Variant Interpreter uses fuzzy matching, thus providing potentially related genes. This functionality does not omit any genes but does return additional genes. |
| **BSVI-12422** | Import | If a user tries to upload a VCF file that is not properly formatted, the upload fails with an ambiguous error message. The file shows a status of fail, and the user can then delete it. Consequently, the variant grid does not appear.

Note: If you experience a failed upload and reuploading the data does not resolve the issue, contact support. |
| **ON-345** | Subject phenotypes | Autocomplete box shows results marked as obsolete by nomenclature authority.

This functionality is intended, Variant Interpreter does not support obsolete/legacy ontology terms. |
| **ON-516** | Subject phenotypes | Results in autocomplete pop-up might be sorted inconveniently (subjective). Contact support to give feedback if you would like this improved. |

Issue Key	Issue Category	Description
BSVI-21855	Variant Grid	VCF name truncation to analysis result name may not match expectation (subjective). For best results, maintain unique Analysis Result names in Variant Interpreter by keeping VCF file names unique up to the first period in the file. Contact support to give feedback if you would like this improved.
BSVI-24136	Visualization	The mutational signature plot is optimized for WGS, however a plot is not generated for any case with fewer than 200 SNVs. This functionality is intended, Variant Interpreter requires a minimum number of single nucleotide variants to generate a mutational signatures plot. Help documentation has been updated to reflect this.
BSVI-24137	Visualization	The dynamic visualization is located separate from the visualization panel, which can be misleading to users. This functionality is intended, static visualizations and dynamic visualizations are currently separate components within Variant Interpreter. Help documentation has been updated to reflect this.
WAC-767	Workgroups	Workgroup Administrators cannot revoke a pending invitation, however Workgroup Administrators can still remove members from the workgroup. If you would like to revoke an invitation to a workgroup and the user has not yet registered for BaseSpace Variant Interpreter, contact support for assistance.
BSVI-24655	Zygosity	Zygosity text for variants on sex chromosomes does not account for pseudoautosomal regions. This functionality is intended, Variant Interpreter does not yet support PAR regions. Help documentation has been updated to reflect this.
BSVI-24656	Zygosity	Pedigree diagrams reflect familial inheritance only for PASS variants This functionality is intended, Variant Interpreter does not yet support display of non-PASS variants in the pedigree diagram. Help documentation has been updated to reflect this.