ChemoOnto, an ontology to qualify the course of chemotherapies

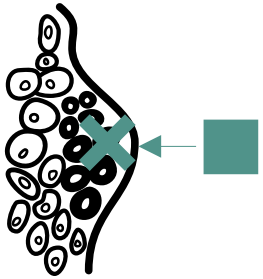
Alice ROGIER, Adrien COULET, Bastien RANCE

Hôpital européen Georges-Pompidou

Context (1/3)

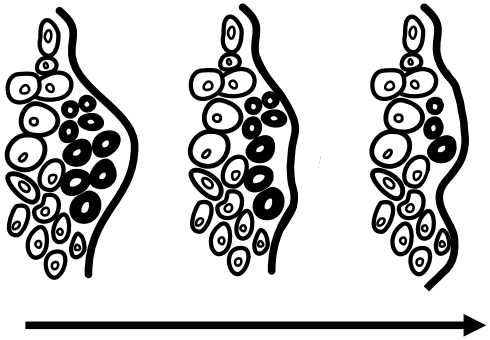
Chemotherapy treatment action and responses

Anti-cancer drugs are cytotoxic molecules

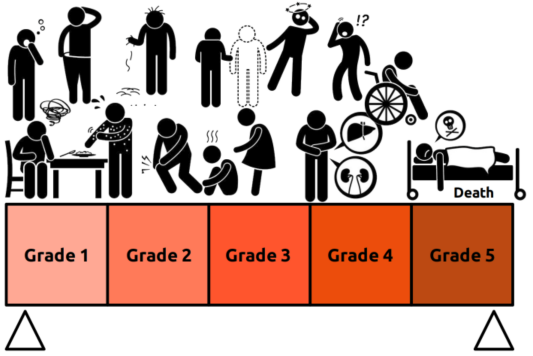


Killing tumor cells

Chemotherapy action



Tumor size



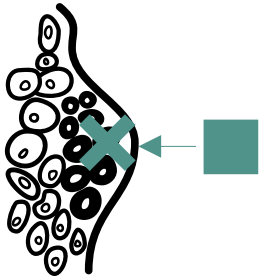
Toxicity event

Chemotherapy responses

Context (1/3)

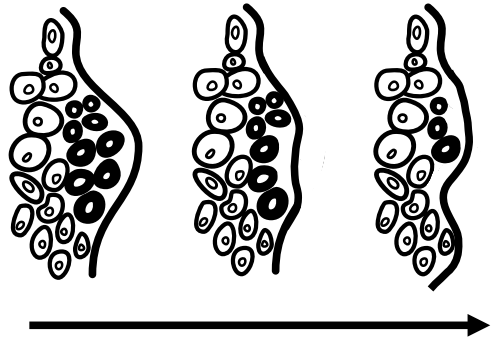
Chemotherapy treatment action and responses

Anti-cancer drugs are cytotoxic molecules



Killing tumor cells

Chemotherapy action



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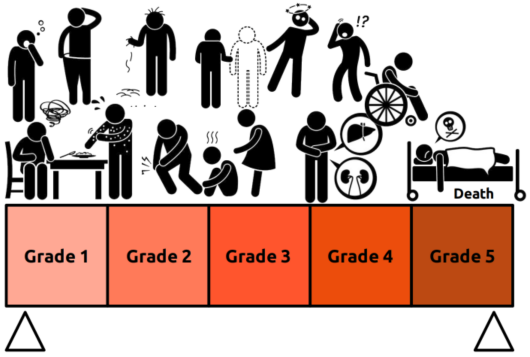

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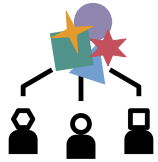
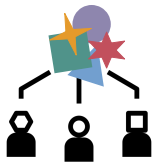


Patient-dependant

Chemotherapy responses

Context (2/3)

Chemotherapy course

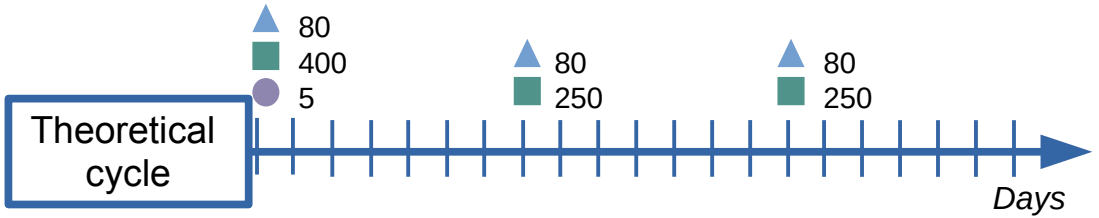


Patient-dependant

Standard Regimens list

Multidisciplinary Team Meeting

Example : Regimen 465 given to ENT cancer patients

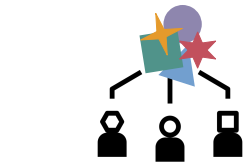


In this theoretical cycle of 21 days, the following molecules are administrated :

- Cetuximab
  day 1 at 400 mg/m²
  day 8 and 15 at 250 mg/m²
- Carboplatine
  day 1 at 5 mg
- Placlitaxel
  day 1, 8 and 15 at 80 mg/m²

Context (2/3)

Chemotherapy course



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Standard Regimens list

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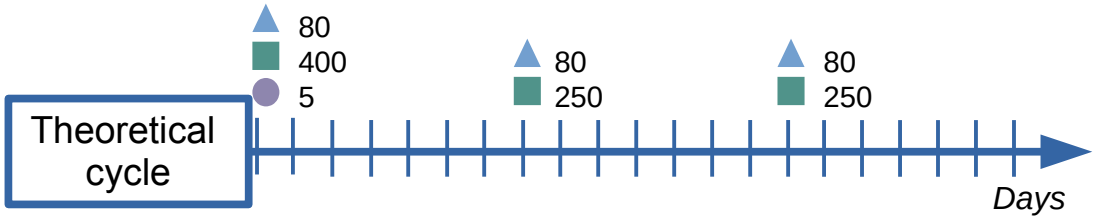

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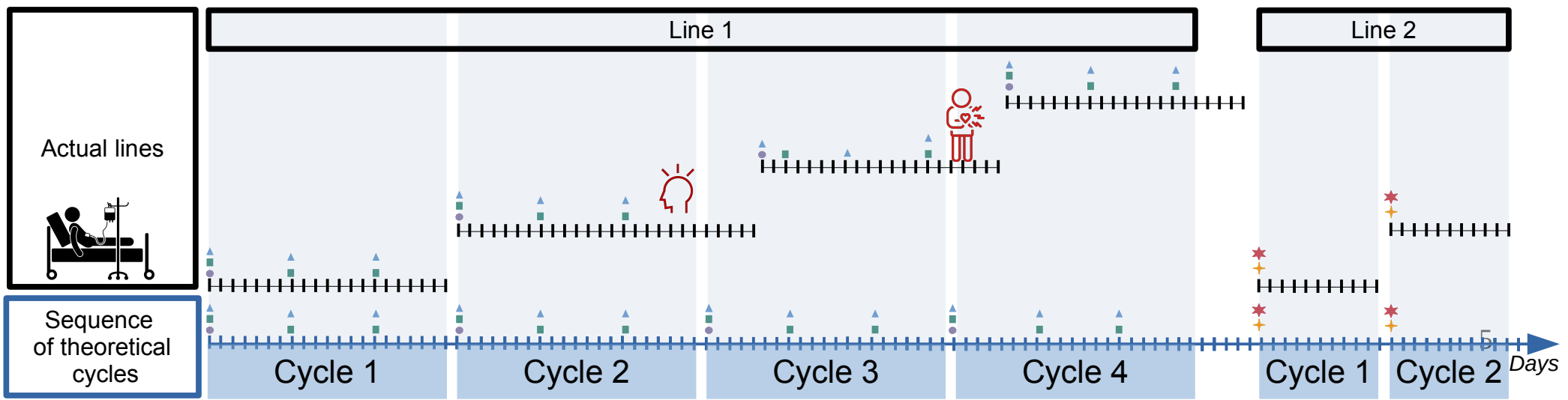
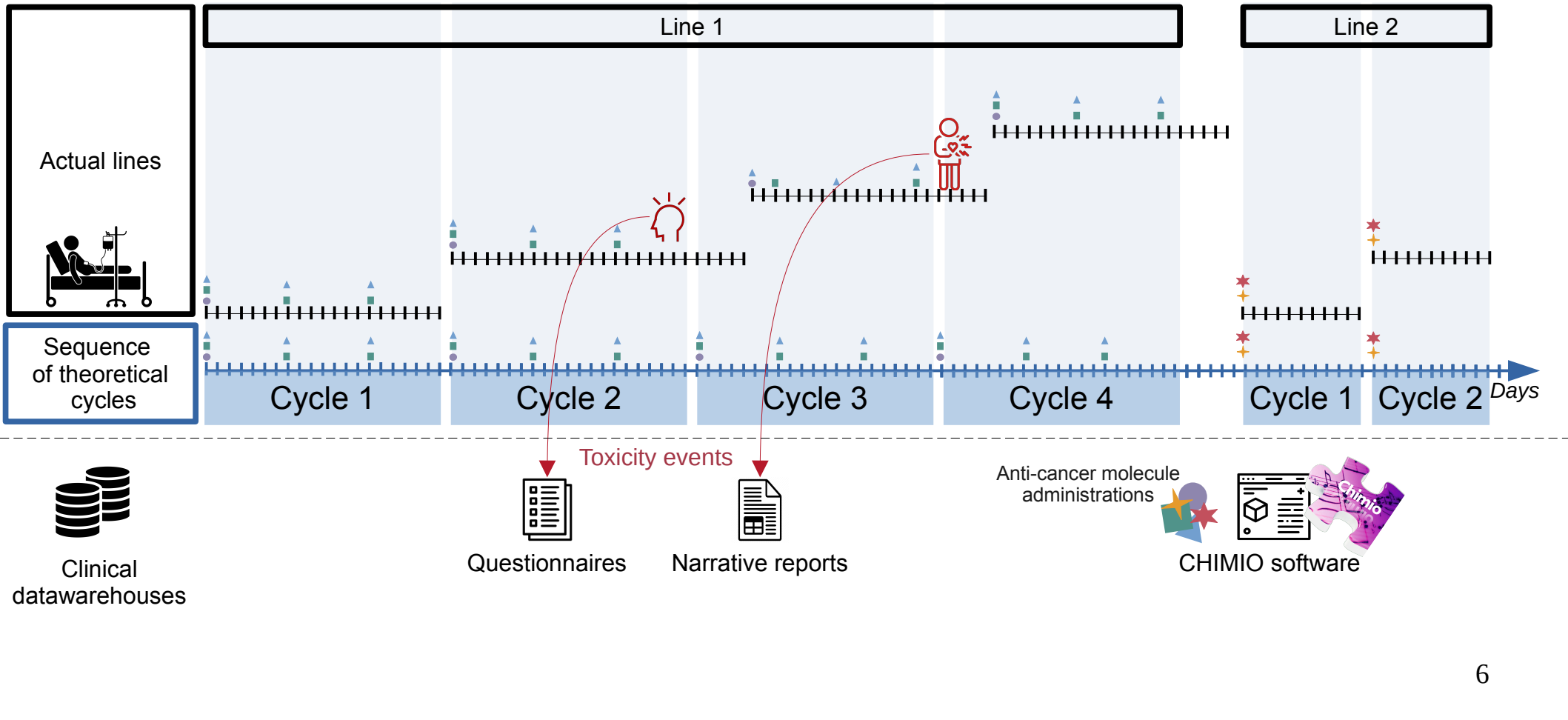


Context (3/3)

Chemotherapy knowledges in clinical datawarehouses



Context (3/3)

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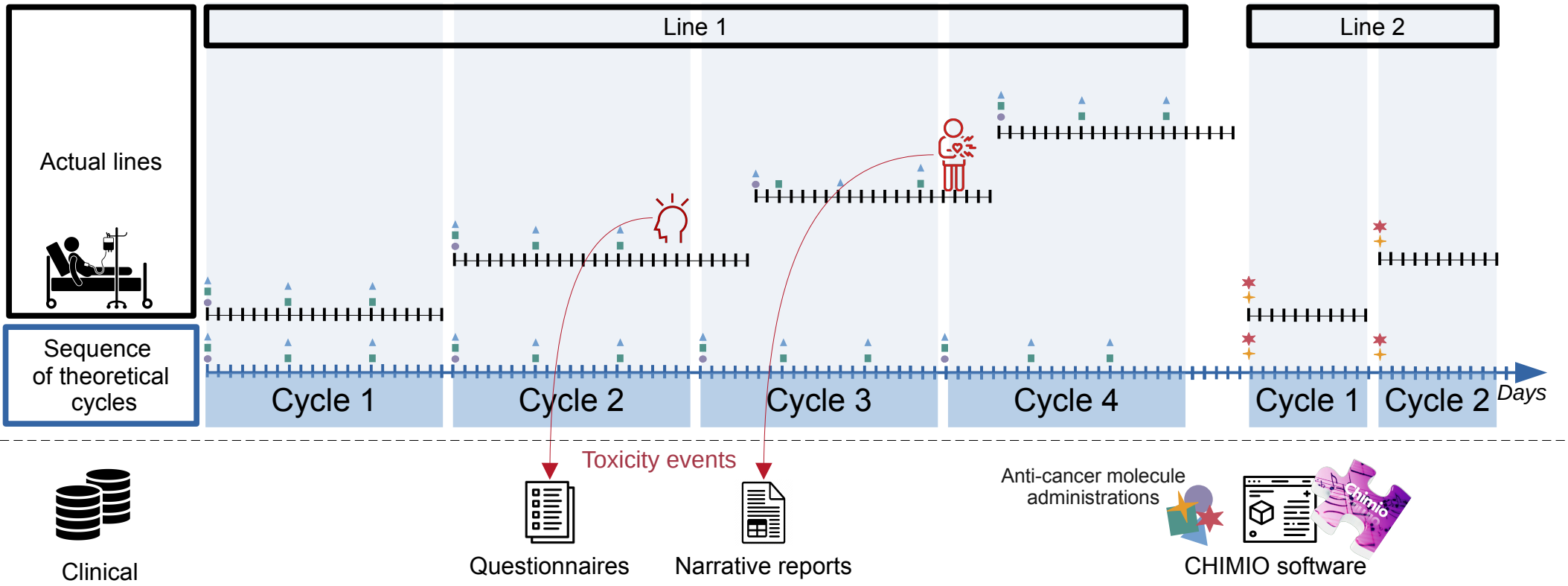
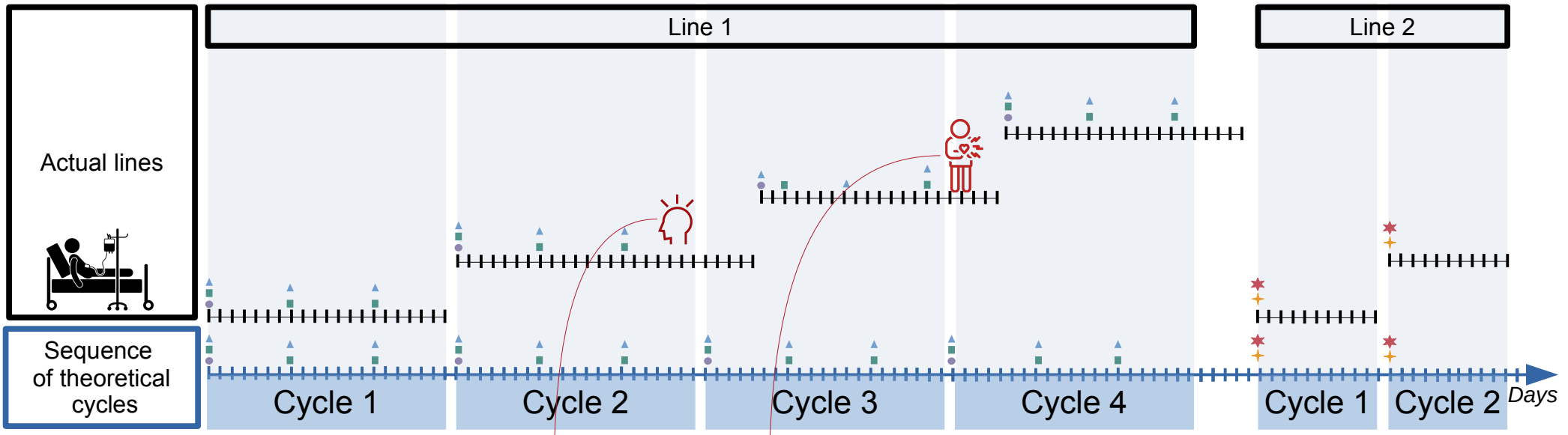


This knowledge:

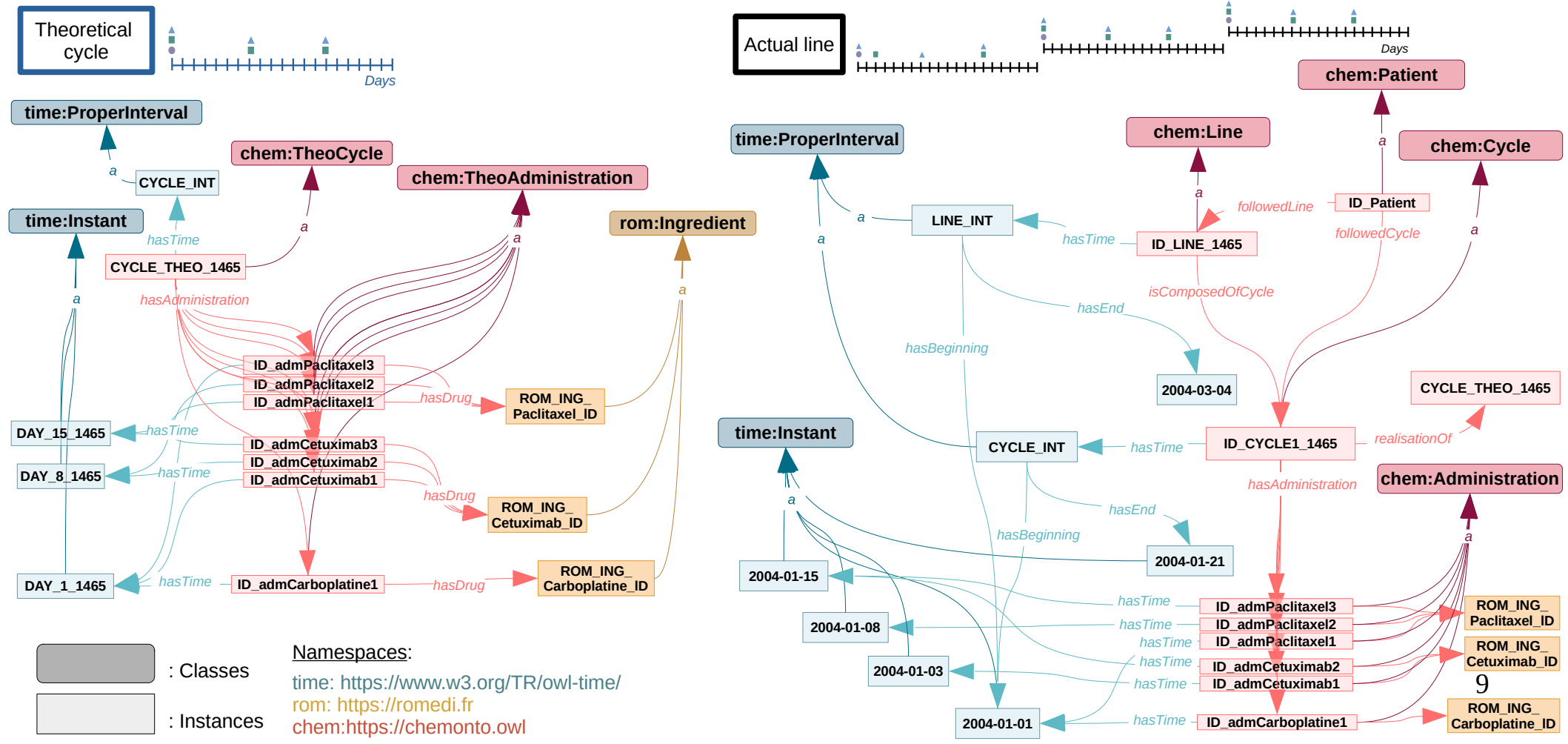
- remains unexploited
- not directly available

Context (3/3)

Chemotherapy knowledges in clinical datawarehouses



ChemoOnto structure, an ontology to… (0/3)



: Classes

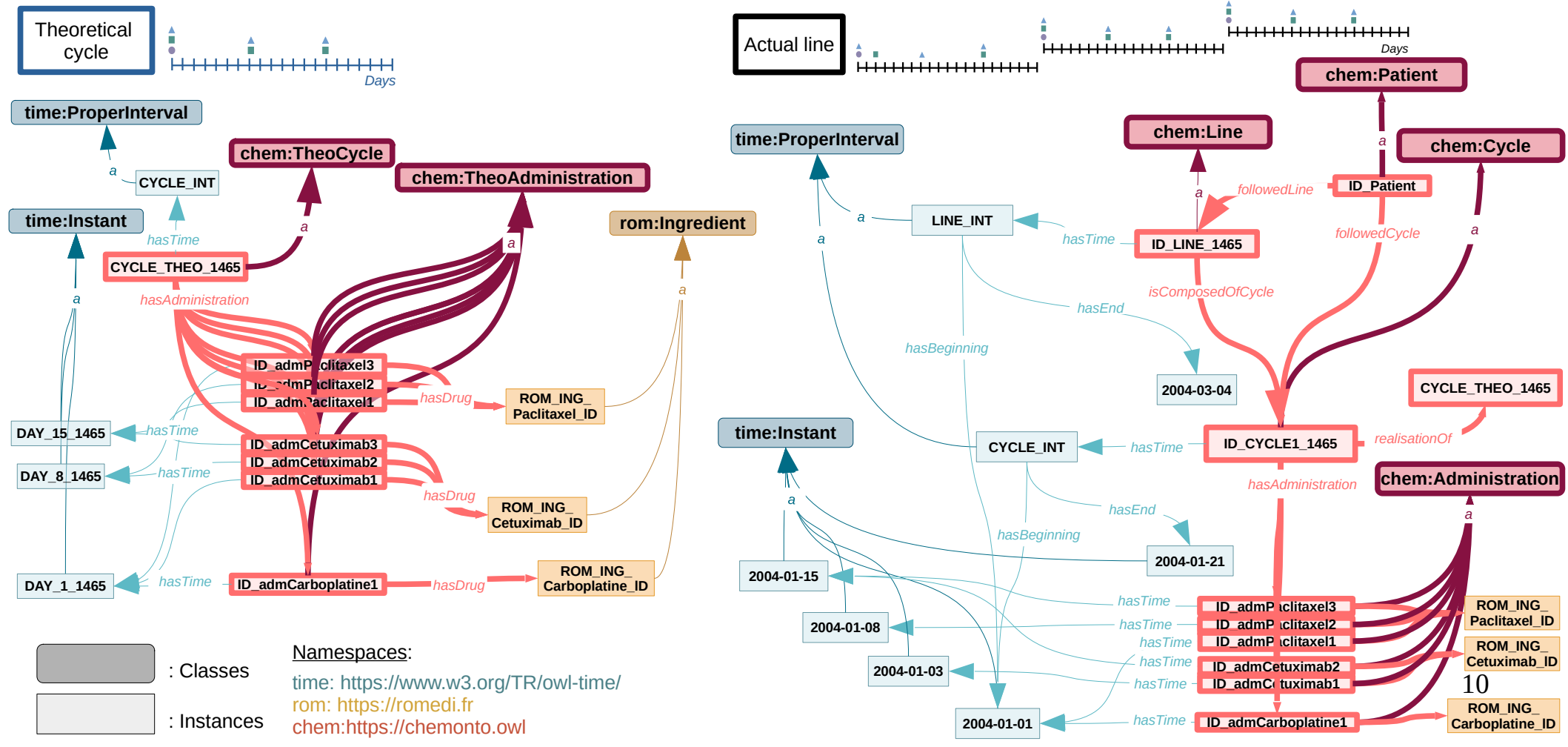
: Instances

Namespaces:

time: https://www.w3.org/TR/owl-time/
rom: https://romedi.fr
chem:https://chemonto.owl

ChemoOnto structure, an ontology to… (1/3)

Represente the complexity of chemotherapy course



ChemoOnto structure, an ontology to… (1/3)

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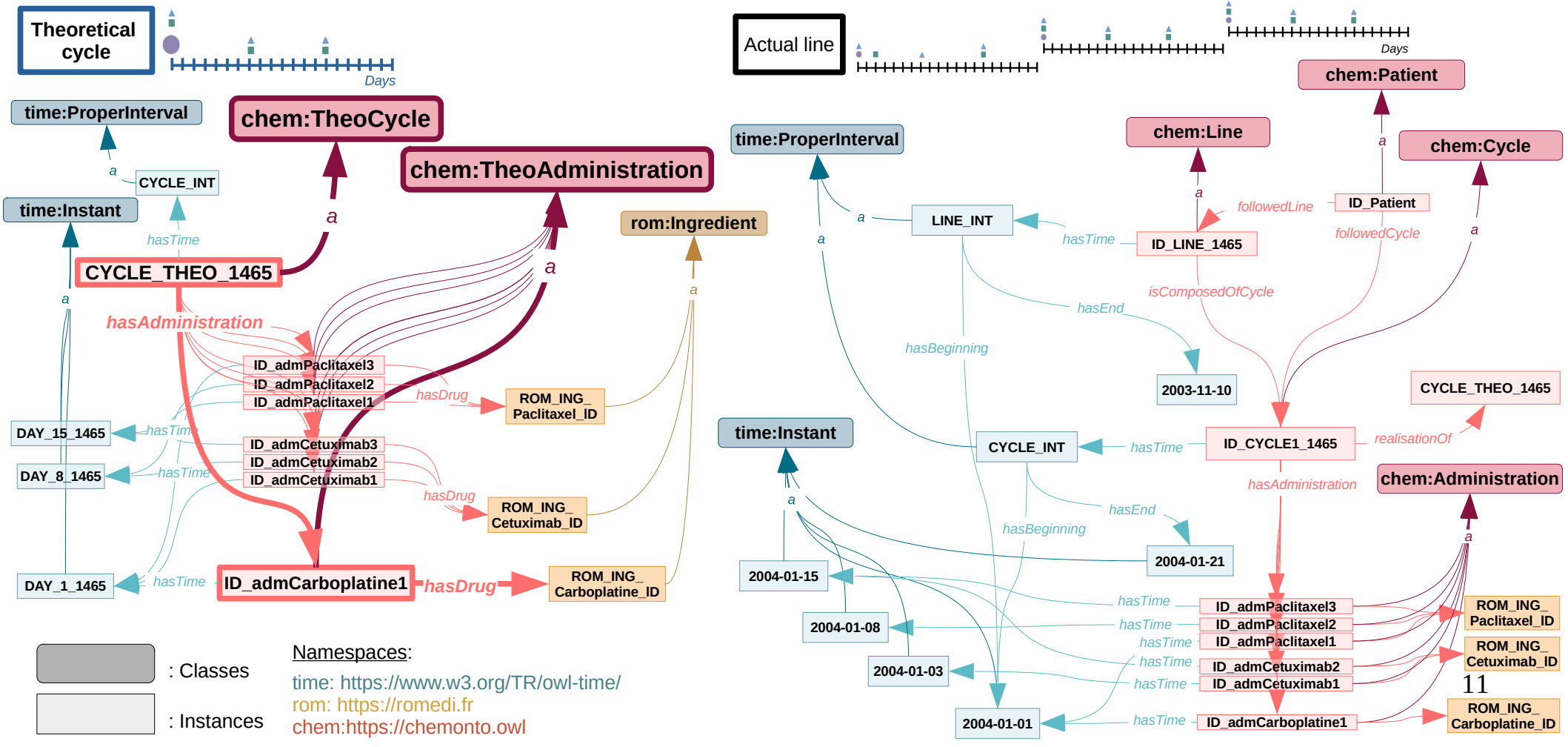
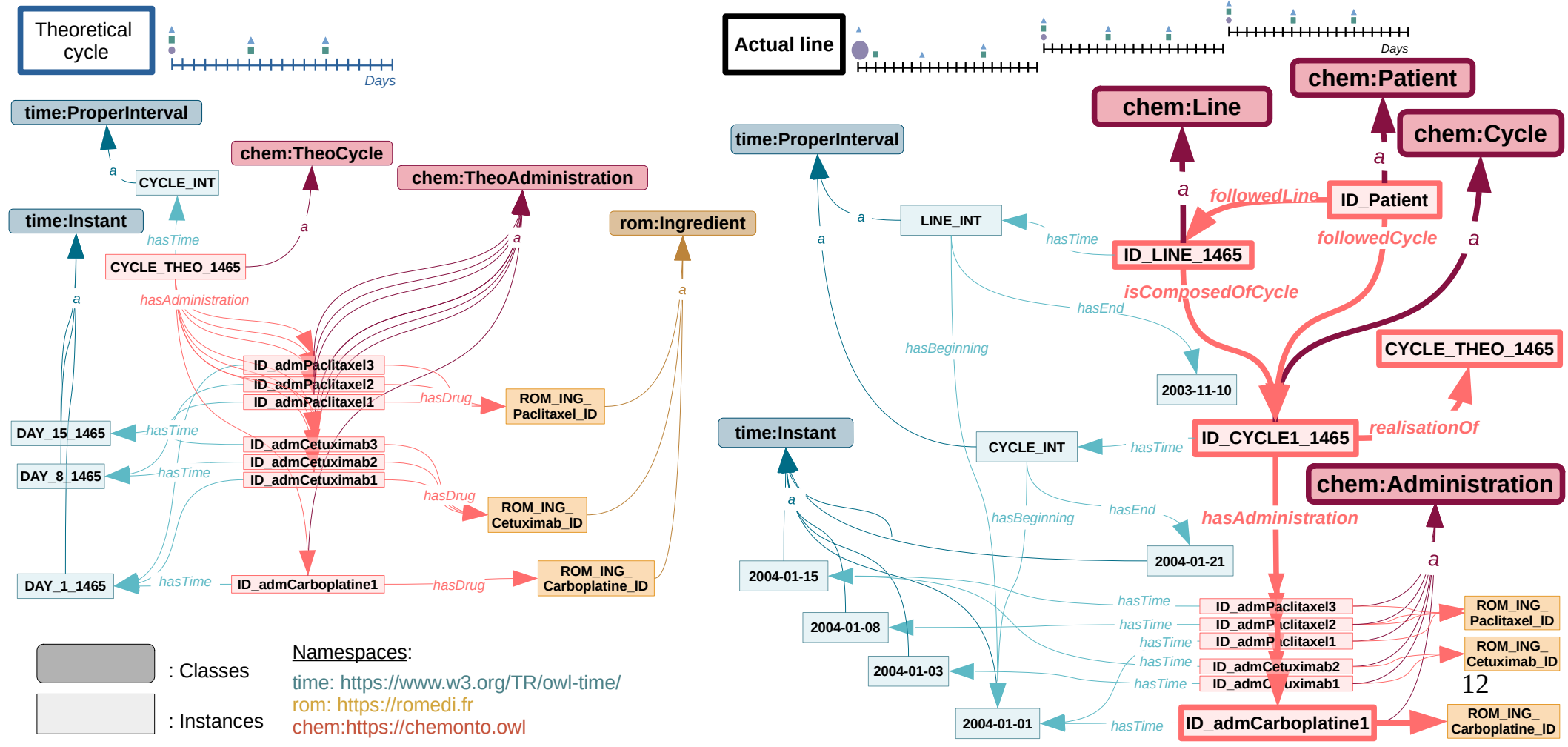


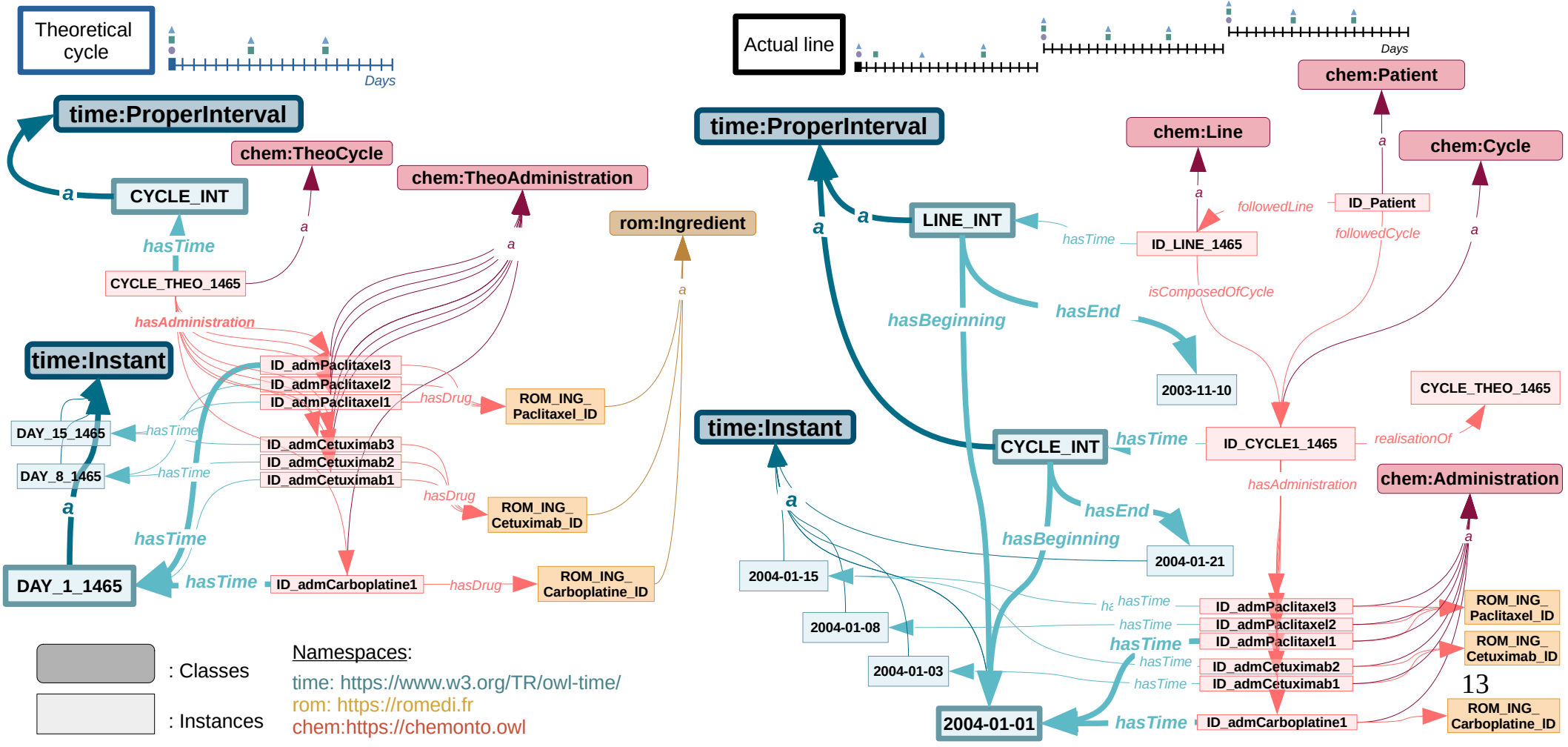
ChemoOnto structure, an ontology to… (1/3)

Represente the complexity of chemotherapy course



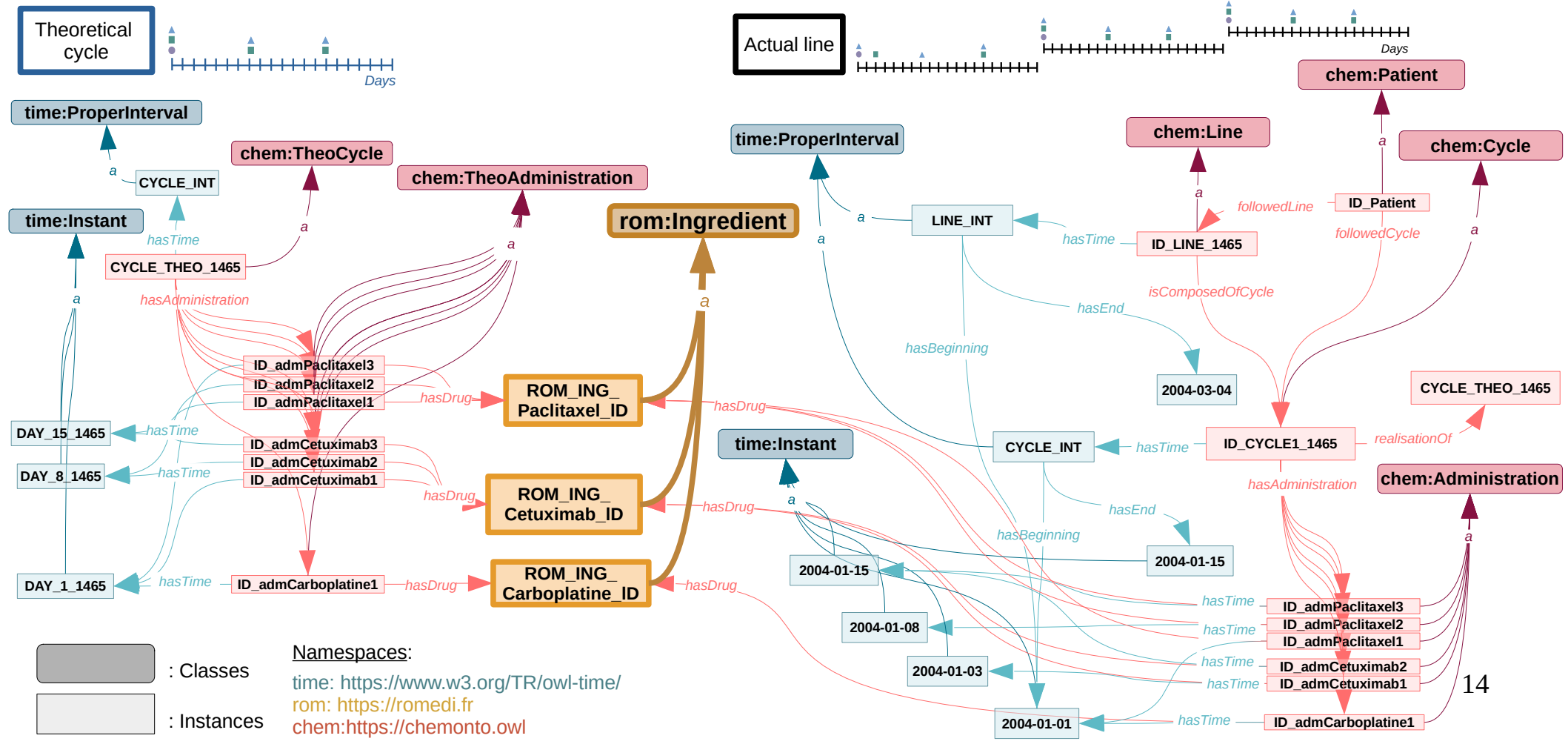
ChemoOnto structure, an ontology to… (2/3)

Link to other knowledge models : the Time Ontology



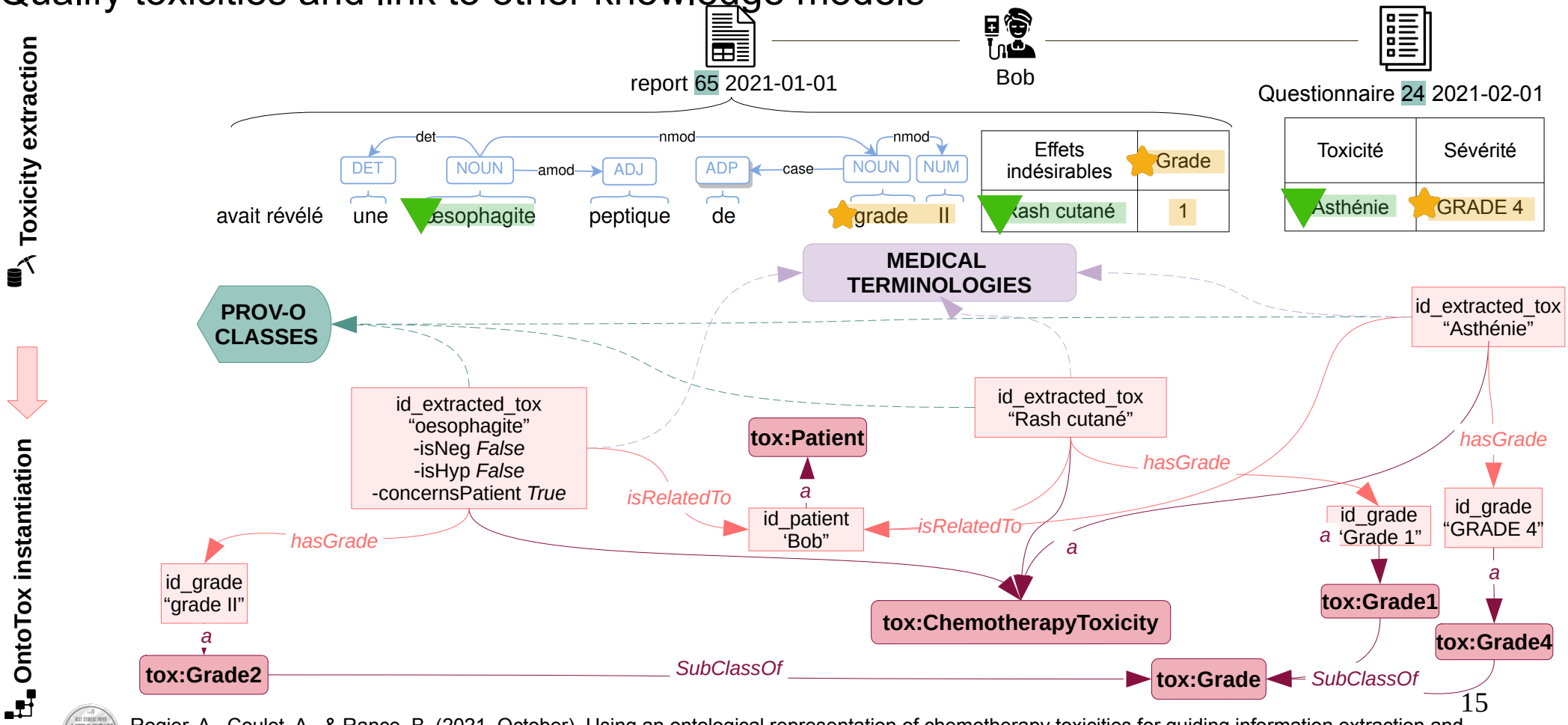
ChemoOnto structure, an ontology to… (2/3)

Link to other knowledge models : Romedi (incl. ATC and RxNorm)



OntoTox structure, an ontology to… (1-2/3)

Qualify toxicities and link to other knowledge models

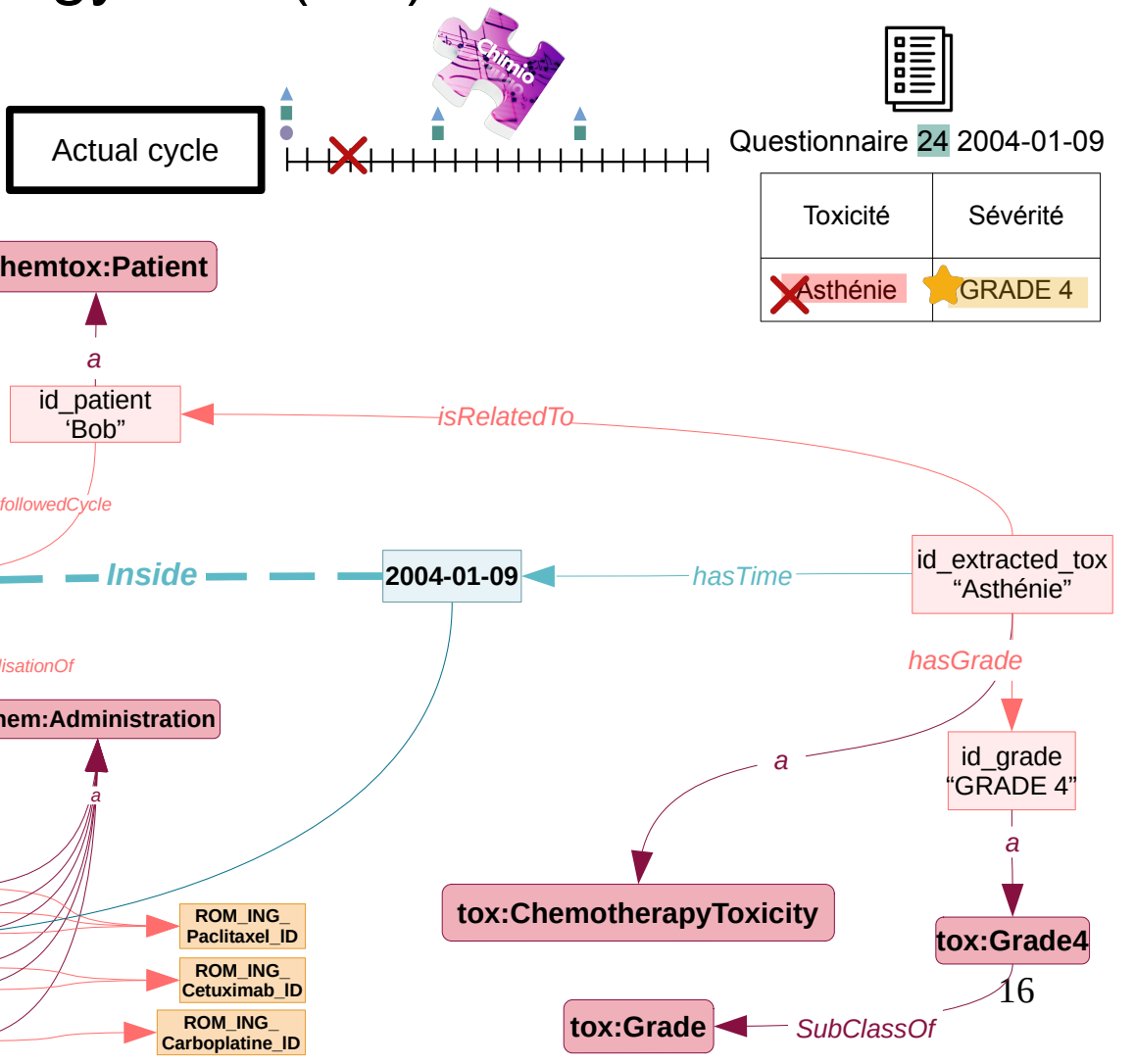


Rogier, A., Coulet, A., & Rance, B. (2021, October). Using an ontological representation of chemotherapy toxicities for guiding information extraction and integration from EHRs. In Medinfo 2021-18th World Congress on Medical and Health Informatics

ChemoOnto structure, an ontology to… (3/3)

Reasone with SWRL rules

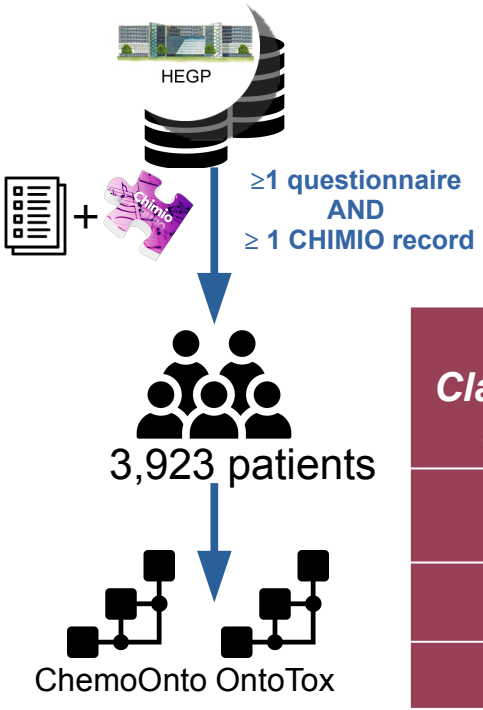
```
SWRL rule :
chemtox:Patient(?pat),
chem:Cycle(?cycle),
tox:ChemotherapyToxicity(?tox),
time:ProperInterval(?p),
time:Instant(?i),
chem:followedCycle(?pat, ?cycle),
tox:isRelatedToPatient(?tox, ?pat),
time:hasTime(?cycle,?p),
time:hasTime(?tox,?i),
time:inXSDDateTime(?i,?di),
time:hasBeginning(?p, ?pbeg),
time:hasEnd(?p,?pend),
time:inXSDDateTime(?pbeg, ?dpbeg),
time:inXSDDateTime(?pend, ?dpend),
swrlb:lessThanOrEqual(?dpbeg, ?di),
swrlb:lessThanOrEqual(?di, ?dpend)
-> time:inside(?p,?i)
```



Relevance of using ontologies to represente chemotherapy responses

Why using ontologies ?	ChemoOnto	OntoTox
1.Representing complexity	-agreing on a specific model -representing actual and theoretical treatment regimens chem:TheoAdministration chem:Administration chem:TheoCycle chem:Cycle chem:Line	-agreing on a specific model -qualifying chemotherapy toxicity and their severity tox:ChemoterapyToxicity tox:Grad
2.Linking to other knowledge models	-representing time with the Time Ontology -representing drugs with Romedi time:ProperInterval Romedi Ingredients time:Instant	-encoding data provenance with PROVO -normalizing toxicity extractions with medical ontologies MEDICAL TERMINOLOGIES PROV-O CLASSES
3.Reasoning	Levegaring temporal reasoning rule to enriche chemotherapy knowlegde	

Use Case: ChemoOntoTox instantiation



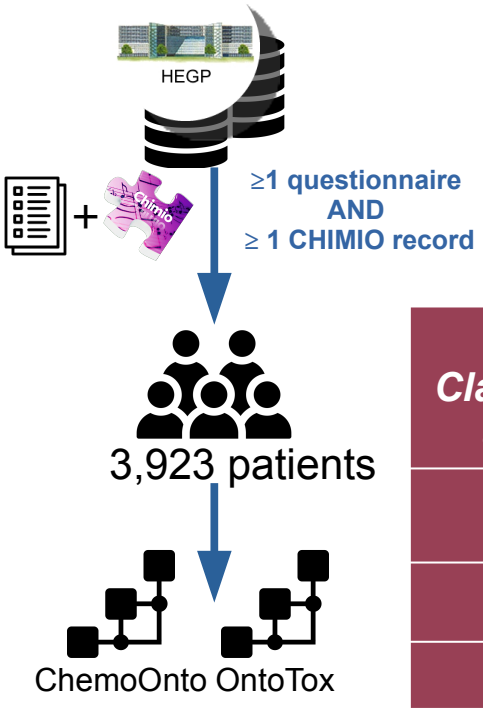
ChemoOnto Classes representing theorethical regimens	#instances
TheoAdministration	6,056
TheoCycle	1,973

ChemoOnto Classes representing actual treatment	#instances
Administration	487,325
Cycle	62,343
Line	11,197

OntoTox Classes	#instances
ChemotherapyToxicity	980,105
Toxicity evaluated as absent	759,622
Toxicity evaluated with its severity	220,483

time:inside object property	#instances
Toxicity instant indentified within a cycle interval	825,202
Toxicity evaluated as absent instant indentified within a cycle interval	633,766
Toxicity evaluated with its severity instant indentified within a cycle interval	191,436

Use Case: ChemoOntoTox instantiation



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Conclusion

Why using ontologies ?	ChemoOnto	OntoTox
1.Representing complexity	-agreing on a specific model -representing actual and theoretical treatment regimens	-agreing on a specific model -qualifying chemotherapy toxicity and their severity
2.Linking to other knowledge models	-representing time with the Time Ontology -representing drugs with Romedi	-encoding data provenance with PROVO -normalizing toxicity extractions with medical ontologies
3.Reasoning	Levegaring temporal reasoning rule to enriche chemotherapy knowlegde	

Overlooks :
-Studying chemotherapy responses with ChemoOnto and OntoTox
-Exporting models in other hospitals

Thank you !



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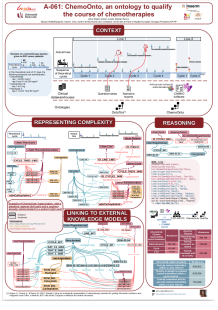
ChemoOnto GitHub:
https://github.com/TeamHeka/ChemoOnto



Presenting poster A-061

Bibliography :

Touré, V.; Krauss, P.; Gnodtke, K.; Buchhorn, J.; Unni, D.; Horki, P.; Raisaro, J. L.; Kalt, K.; Teixeira, D.; Crameri, K.; Österle, S. FAIRification of Health-Related Data Using Semantic Web Technologies in the Swiss Personalized Health Network. *Sci Data* **2023**, *10* (1), 127. https://doi.org/10.1038/s41597-023-02028-y.

Warner, J. L.; Dymshyts, D.; Reich, C. G.; Gurley, M. J.; Hochheiser, H.; Moldwin, Z. H.; Belenkaya, R.; Williams, A. E.; Yang, P. C. HemOnc: A New Standard Vocabulary for Chemotherapy Regimen Representation in the OMOP Common Data Model. *Journal of Biomedical Informatics* **2019**, *96*, 103239. https://doi.org/10.1016/j.jbi.2019.103239.

Cossin, S.; Lebrun, L.; Lobre, G.; Loustau, R.; Jouhet, V.; Griffier, R.; Mougin, F.; Diallo, G.; Thiessard, F.
Romedi: An Open Data Source About French Drugs on the Semantic Web. *Stud Health Technol Inform* **2019**, *264*, 79–82. https://doi.org/10.3233/SHTI190187.

Rogier, A.; Coulet, A.; Rance, B.
Using an Ontological Representation of Chemotherapy Toxicities for Guiding Information Extraction and Integration from EHRs. *Stud Health Technol Inform* **2022**, *290*, 91–95. https://doi.org/10.3233/SHTI220038.

Batsakis, S.; Stravoskoufos, K.; Petrakis, E. G. M.
Temporal Reasoning for Supporting Temporal Queries in OWL 2.0. In *Knowledge-Based and Intelligent Information and Engineering Systems*; König, A., Dengel, A., Hinkelmann, K., Kise, K., Howlett, R. J., Jain, L. C., Eds.; Lecture Notes in Computer Science; Springer: Berlin, Heidelberg, 2011; pp 558–567. https://doi.org/10.1007/978-3-642-23851-2_57.

```
SELECT ?tox_id ?tox_label ?tox_grade_type ?tox_day ?tox_date ?cycle_id ?cycle_label ?
cycle_num ?cycle_startdate ?type_cui ?qst
      {
    ?tox_id rdfs:label ?tox_label.
    ?tox_id tox:hasGrade ?tox_grade.
    ?tox_grade a ?tox_grade_type.
    ?tox_id time:hasTime ?tox_day.
    ?tox_id a ?type_cui.
    ?tox_day time:inXSDDate ?tox_date.
    ?cycle_id time:hasTime ?cycle_int.
    ?cycle_id rdfs:label ?cycle_label.
    ?cycle_id chem:hasCycleNum ?cycle_num.
    ?cycle_int time:inside ?tox_day.
    ?cycle_int time:hasBeginning ?cycle_beg.
    ?cycle_beg time:inXSDDate ?cycle_startdate.
    FILTER( STRSTARTS(STR(?tox_grade_type),str(tox:)))
    FILTER( STRSTARTS(STR(?type_cui),str(pcui:)))
    FILTER(?cycle_id=<http://chemonto.owl/#CYCLE_2198_xxxxxxx_2017-08-22_2>)
      }
```

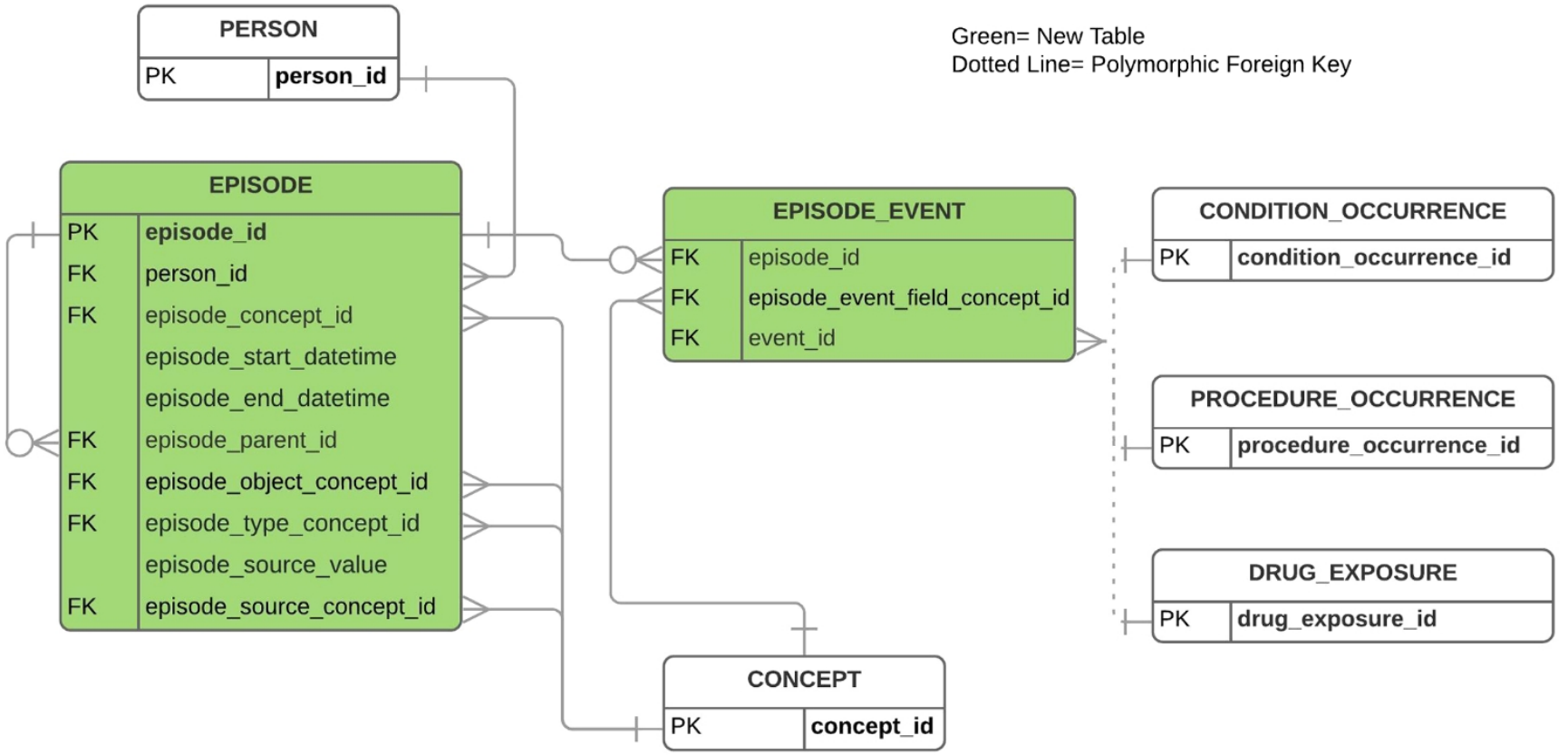


Fig. 1. OHDSI Oncology CDM Extension Proposal data model. HemOnc oncology drug regimen concepts should be assigned in the episode_object_concept_id column of the EPISODE table. FK: foreign key; PK: primary key.

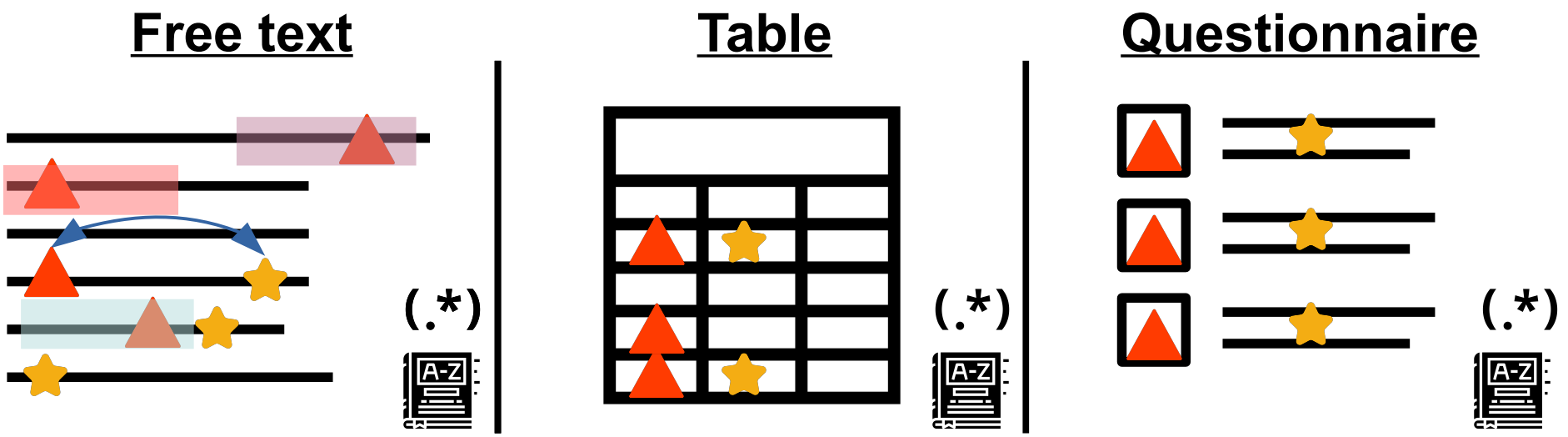
Warner, J. L.; Dymshyts, D.; Reich, C. G.; Gurley, M. J.; Hochheiser, H.; Moldwin, Z. H.; Belenkaya, R.; Williams, A. E.; Yang, P. C. HemOnc: A New Standard Vocabulary for Chemotherapy Regimen Representation in the OMOP Common Data Model. *Journal of Biomedical Informatics* **2019**, *96*, 103239. https://doi.org/10.1016/j.jbi.2019.103239.

FAIR principles	SPHN RDF Schema	SPHN compliant data
F1 Unique identifier	URIs for data elements and for external terminologies	URIs for data instances
F2 Rich metadata	Metadata for data elements	Administrative and descriptive metadata
F3 Linking data and metadata	SPHN RDF properties	SPHN RDF properties
F4 Metadata searchable	Schema dereferenceable on the web (open access)	Administrative metadata is searchable within a project (restricted access)
A1.1 Open communication protocol	HTTPS protocol	SPARQL queries
A1.2 Authentication protocol		SWITCH edu-ID to access the projects B-space on BioMedIT
A2 Long term availability	Available on the website and GitLab	Depends on the data provider and project agreement
I1 Knowledge representation	RDF	RDF
I2 Controlled vocabulary	Meaning binding to SNOMED CT and LOINC Defined list of allowed value sets	Mapping between local codes and standards
I3 Linked data	SPHN and standard RDFS/OWL properties (i.e., rdfs:domain, rdfs:range, owl:equivalentClass, owl:Restriction)	SPHN RDF properties
R1.1 Data usage licence	CC BY 4.0	Individual datasets have their own licence
R1.2 Detailed provenance	Concepts and properties to represent administrative metadata (e.g. extraction datetime, data provider institute)	Administrative and descriptive metadata (e.g. extraction datetime, data provider institute)
R1.3 Community standards	SKOS, Dublin Core (e.g. skos:note, dc:description, dc:title, dct:license)	

Table 1. FAIR principles satisfied in the SPHN RDF Schema and data.

Touré, V.; Krauss, P.; Gnodtke, K.; Buchhorn, J.; Unni, D.; Horki, P.; Raisaro, J. L.; Kalt, K.; Teixeira, D.; Crameri, K.; Österle, S. FAIRification of Health-Related Data Using Semantic Web Technologies in the Swiss Personalized Health Network. *Sci Data* **2023**, *10* (1), 127. https://doi.org/10.1038/s41597-023-02028-y.

Toxicity extraction processes



Entity recognition :

: toxicity ------- : 4,038 toxicity term dictionary

: grade ------- (.*) : regular expression

Context detection:

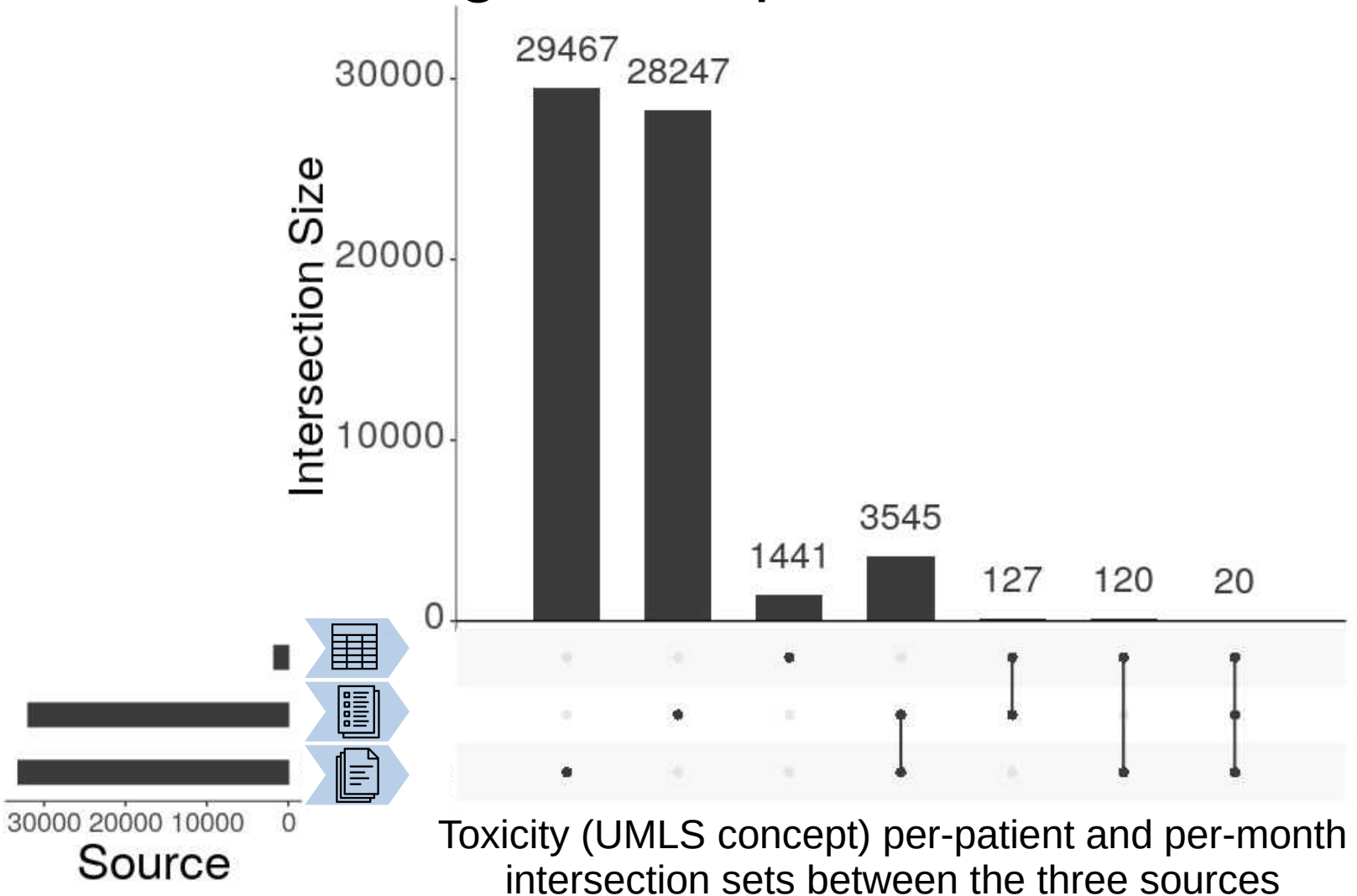
negation

hypothesis

family

: Link between entities with dependency parsing

Results for 330 lung cancer patients



Toxicity (UMLS concept) per-patient and per-month intersection sets between the three sources