Expert opinion in human genetics

BRCA1 reclassification and failure to notify

A hypothetical BRCA1 splice variant reported in 2017 as a variant of uncertain significance is upgraded internally by the laboratory in 2021, no updated report is issued, and in February 2024 the patient is diagnosed with advanced ovarian cancer.



Fictitious sample case – the specific case, the persons, the events and the instruction are simulated. This is not a real expert opinion. Cited literature, guidelines and database entries are real and given with the date they were checked.

Field	Medical liability · Laboratory diagnostics in human genetics
Instructed by	Regional Court (Landgericht) [fictitious], 6th Civil Chamber
Case number	6 O 87/25 [fictitious]
Person concerned	Claimant S. W. [fictitious], born 19 January 1978
Expert	**Prof. Dr. med. Christian T. Thiel-Hirschmann, MBA** Specialist in Human Genetics, Adjunct Professor at Friedrich-Alexander-Universität Erlangen-Nürnberg
Date	8 November 2026
Key question	Was the classification of the variant as uncertain in 2017 justifiable, from when did the available evidence support an upgrade, what was professionally recommended for communicating a reclassification, and what can be said medically about the hypothetical course had the information been available in time?

1. Instruction and questions put by the court

By order for the taking of evidence (Beweisbeschluss) of 15 July 2026, the 6th Civil Chamber of the Regional Court (Landgericht) [fictitious] instructed the undersigned to provide an expert opinion in human genetics in the proceedings brought by the claimant S. W. [fictitious] against the medical care centre for human genetics (MVZ für Humangenetik) [fictitious]. The claimant contends that a *BRCA1* variant detected in 2017 was wrongly classified and that a later upgrade was not communicated to her, as a result of which she was denied risk-reducing surgery and developed ovarian cancer in 2024. The defendant considers the 2017 classification to have been correct and denies any duty to inform patients, unprompted and years later, of new findings.

The Chamber has put the following questions:

1. Did the classification of the *BRCA1* variant as a variant of uncertain significance (class 3) in the report of 22 May 2017 correspond to the professional standard of laboratory diagnostics in human genetics at that time?
2. From what point in time was there knowledge that would professionally have supported an upgrade to class 4 (likely pathogenic) or class 5 (pathogenic)?
3. What requirements did the medical and professional standard in the years 2017 to 2024 place on the reassessment of variants already reported and on the communication of a reclassification?
4. What measures would have been recommended to the claimant had she known of a likely pathogenic or pathogenic *BRCA1* variant in 2017 or in 2021 respectively?
5. With what probability would the ovarian cancer diagnosed in February 2024 have been avoided or detected at an earlier stage had these measures been carried out?
6. Does the late knowledge give rise to further health disadvantages, in particular with regard to breast cancer surveillance?

2. Preliminary remarks of the expert

Note on the fictitious sample case

This expert opinion is a fictitious sample case. The court, parties, persons, instruction, file contents and events are simulated. The *BRCA1* variant is hypothetical and is deliberately given without a complete HGVS designation as c.[…]+5G>A. Its classification history, the database extracts, the RNA results and the classification by the expert panel are facts set for the fictitious file. They do not describe any real variant or database history and cannot be independently verified. The cited literature, standards and statutory provisions have been checked.

Independence and review of the instruction. In accordance with § 407a(1) ZPO (German Code of Civil Procedure), the undersigned has examined whether the instruction falls within his field of expertise. He comments on the treatment and prognosis of ovarian cancer only insofar as this is necessary for the assessment of causation, and for that purpose suggests, if appropriate, an additional expert opinion in gynaecological oncology. There are no grounds that could justify doubts as to his impartiality (§ 407a(2) ZPO). The undersigned has not previously counselled or examined the claimant and has no relationship with the parties.

Role and limits. The undersigned answers medical questions. Whether there has been a breach of duty in the legal sense, which duties to communicate existed, how the claimant would have decided and whether any damage is compensable are for the Chamber to decide. The same applies to the final assessment of causation and to the question of whether § 286 ZPO or § 287 ZPO governs it. The undersigned states medical probabilities in grades: **possible** means that something cannot be ruled out but is not more likely than the alternative, and **more likely than not** means that, from a medical point of view, more speaks for it than against it. These grades describe a professional assessment, not an evaluation of evidence.

Reference date. The benchmark for questions 1 to 3 is the evidence and the rules at the respective point in time. The undersigned distinguishes the date on which new evidence became available from the date of a formal classification by a laboratory or an expert body.

Methodology. Review of the file including the defendant's internal classification documentation and dated database extracts, assessment of criteria according to the ACMG/AMP standard of 2015 together with the recommendations of the ClinGen Sequence Variant Interpretation Working Group and the gene-specific specifications of the ClinGen ENIGMA expert panel for *BRCA1* and *BRCA2*, comparison with the consensus recommendations of the German Consortium for Hereditary Breast and Ovarian Cancer. Database classifications are presented separately from the undersigned's own assessment of criteria. Literature search in PubMed up to November 2026. A personal examination was not required.

3. Documents

- Court file with statement of claim of 4 April 2025, defence of 30 June 2025 and reply of 2 September 2025
- Counselling letter of the defendant of 14 March 2017 with pedigree
- Report of the defendant of 22 May 2017 (multigene panel, referring physician Dr B. [fictitious]) and results discussion letter of 13 June 2017
- Internal classification documentation of the defendant, versions of 22 May 2017 and 18 March 2021
- Standard operating procedure of the defendant "Reassessment of variants", version 2.0 of 1 July 2019
- Dated printouts of ClinVar entries for the variant (May 2017, October 2020, March 2021, May 2025), the content of which is set for this sample case
- Reports of the intensified breast cancer surveillance of the breast centre [fictitious] 2017 to 2023
- Operation report, histopathology and discharge letter, February 2024
- Tumour genetic report of 21 March 2024, germline report of the university hospital [fictitious] of 26 April 2024
- Letter from the gynaecological oncology outpatient clinic [fictitious] of 17 September 2026

4. Facts of the case

4.1 Family history and report 2017

In March 2017 the claimant was 39 years old and healthy. Her mother had developed breast cancer at 44 years and died at 52 years. The mother's sister had developed ovarian cancer at 56 years and died two years later. Material from the deceased was not available. The claimant has two children, born in 2007 and 2010. The counselling letter of 14 March 2017 documents completed family planning and the undisputed fulfilment of the German Consortium's inclusion criteria for germline testing.

Counselling and the results discussion took place in the defendant's genetic counselling clinic and were conducted by the specialist in human genetics Dr B. [fictitious]. As the responsible physician she requested the analysis in the defendant's laboratory and is named in the report as the referring physician.

For this sample case it is assumed that the laboratory detected, in the heterozygous state, an intronic variant at position +5 of the splice donor site of a *BRCA1* intron, referred to here as *BRCA1* c.[…]+5G>A. The report of 22 May 2017 classified it as class 3 and stated: "Predictive testing of relatives for this variant is not recommended. Surveillance is based on the family history." Neither the report nor the

results discussion letter contains any reference to possible changes in the classification or any recommendation to make a later enquiry. On the basis of the family history, intensified breast cancer surveillance at a centre was recommended. A risk-reducing salpingo-oophorectomy was stated to be "not currently indicated in the absence of a pathogenic variant".

4.2 Course 2017 to 2023

From July 2017 to October 2023 the claimant took part in intensified surveillance with annual MRI and six-monthly ultrasound. All findings were unremarkable.

According to the database extract of October 2020 contained in the file, a university laboratory [fictitious] deposited results of an RNA analysis in another carrier. According to these, the variant leads to skipping of the preceding exon with a frameshift, and no normal transcript from the variant allele was detectable. The laboratory classified the variant as likely pathogenic.

On 18 March 2021 the defendant detected the same variant in another patient, reassessed it with reference to these RNA data and classified it as class 4. The internal database was updated. The defendant's standard operating procedure of 2019 provides: "If a previously reported variant is upgraded to class 4 or 5, the referring physician is informed in writing." No updated report was issued, nor was the referring physician informed. According to the defendant's submission, the case had not been linked to the variant database during the data migration in 2019. For this sample case it is further assumed that the defendant is not one of the centres of the German Consortium.

4.3 Disease 2024

At the beginning of January 2024 the claimant, then aged 45, presented with a feeling of fullness and increasing abdominal girth. On 6 February 2024 a high-grade serous carcinoma of the adnexa, stage FIGO IIIC, was diagnosed. This was followed by surgery with no macroscopic residual tumour, chemotherapy and PARP inhibitor maintenance until February 2026. There is currently no evidence of recurrence. In May 2024, on enquiry, the claimant learned of the defendant's upgrade in 2021.

5. Findings

Date	Source	Content
22.05.2017	Germline report of the defendant	*BRCA1* c.[…]+5G>A heterozygous, class 3
October 2020	Database extract (fact of the case)	RNA data of a university laboratory, classification likely pathogenic
18.03.2021	Internal reassessment by the defendant	Class 4, no updated report, referring physician not informed
2017 to 2023	Intensified surveillance	Breast MRI and ultrasound unremarkable throughout
06.02.2024	Histopathology	high-grade serous carcinoma of the adnexa, FIGO IIIC
21.03.2024	Tumour genetics	Variant with an allele fraction indicating loss of the wild-type allele, homologous recombination deficiency (HRD) positive
26.04.2024	Germline report university hospital	same variant, internal laboratory classification as class 5

Date	Source	Content
May 2025	Database extract (fact of the case)	Classification as pathogenic by the ClinGen ENIGMA expert panel

The internal laboratory documentation of May 2017 cites as evidence the absence of the variant from large population databases, the concordant prediction of a weakened splice donor site by several programs and a database entry from another laboratory (uncertain, without data). RNA, cosegregation or literature data were not available. The documentation of March 2021 derives class 4 from the RNA results. The report of April 2024 justifies class 5 with RNA data and the tumour findings, without a complete listing of criteria.

6. Scientific background

6.1 BRCA1 and disease risks

Pathogenic germline variants in *BRCA1* give rise to an autosomal dominantly inherited, greatly increased risk of breast and ovarian cancer. In a prospective cohort of 9,856 carriers of pathogenic *BRCA1* or *BRCA2* variants, the cumulative risk to age 80 years for *BRCA1* was 72 per cent for breast cancer and 44 per cent for ovarian cancer (95 per cent confidence interval 36 to 53 per cent). Of the participants, 94 per cent were recruited through family cancer clinics [1].

6.2 Classification systems

The five-tier system proposed in 2008 by an IARC working group defines class 5 as a probability of pathogenicity above 99 per cent, class 4 as 95 to 99 per cent and class 3 as 5 to 94.9 per cent. For class 4 the same measures may be recommended as for class 5, for class 3 no predictive testing of relatives takes place. The clinically decisive boundary is that between class 3 and class 4. The initial report should already point out that the classification may change with new evidence [2].

According to the ACMG/AMP standard of 2015, a variant of uncertain significance should not be used for clinical decision-making. Splice prediction programs have a high sensitivity (approximately 90 to 100 per cent) with lower specificity (approximately 60 to 80 per cent), and their concordant prediction counts only as supporting evidence (PP3). The PVS1 criterion applies to canonical splice sites at positions ±1 and ±2 [3]. The ClinGen Sequence Variant Interpretation Working Group has refined PVS1 [4] and in 2023 recommended capturing RNA findings showing loss of function at transcript level with PVS1 at graded strength instead of PS3 [5]. In 2024 the ClinGen ENIGMA expert panel published statistically calibrated, gene-specific rules for *BRCA1* and *BRCA2*, with which 11 of 13 previously uncertain or conflicting variants were classified during piloting [6]. A revised version of the standard (SVC v4) has so far only been available as a draft in the pilot phase and, according to the ClinGen pilot page, is not intended for clinical use. It was not applied.

6.3 Reclassification, reassessment and communication pathway

In a retrospective analysis from a single commercial laboratory with 1.45 million persons tested, 7.7 per cent of unique uncertain variants (2,048 of 26,670) were reclassified. Of these reclassifications, 91.2 per cent were downgrades to benign or likely benign (median time to the amended report 1.17 years) and 8.7 per cent were upgrades to likely pathogenic or pathogenic (median 1.86 years) [7]. The figures describe this data set and are not a general probability for every uncertain variant or every laboratory. The authors themselves regard the transferability as open [7].

The ACMG/AMP standard recommends that laboratories disclose their rules for reanalysis and, for uncertain variants, insofar as they do not actively update them themselves, recommend periodic enquiries to the treating physicians [3]. The ACMG statement of 2019, expressly formulated as voluntary guidance, recommends written reassessment procedures, a note in reports on possible changes and priority communication of reclassifications with a possible impact on management, for example the upgrade of an uncertain variant to likely pathogenic. The trigger may be the renewed detection of the variant in a new case. For laboratory-initiated reassessments, the laboratory should set out when an updated report is issued and to whom, if the referring physician is no longer caring for the patient. The statement regards a routine reassessment of the entire variant inventory as hardly practicable, and it leaves aside the question of who is to initiate a reassessment [8]. The German Consortium has established for its centres an expert group for the classification of uncertain variants and a recall system through which carriers are informed directly of the classification by this group [9].

The recommendations mentioned describe the communication from the laboratory to the referring physician, not directly to the patient [3, 8]. Under § 11 GenDG (German Genetic Diagnostics Act), a facility instructed with the analysis may communicate the result only to the physician who instructed it (subsection 2), and the result is communicated to the person concerned by the responsible physician or the counselling physician (subsection 1). The provision does not expressly regulate duties to communicate a reclassification.

6.4 Risk-reducing salpingo-oophorectomy

According to the consensus recommendations of the German Consortium, risk-reducing salpingo-oophorectomy is an option for carriers of a pathogenic *BRCA1* variant from 35 years and is recommended from 40 years. For carriers of a *BRCA1* variant, the recommendations see increasing evidence that the procedure does not reduce the risk of breast cancer [9].

In a meta-analysis of observational studies, the procedure was associated with a hazard ratio of 0.21 (95 per cent confidence interval 0.12 to 0.39) for ovarian and fallopian tube cancers [10]. In an international registry cohort of 5,783 carriers with a mean follow-up of 5.6 years, the hazard ratio for ovarian, fallopian tube or peritoneal cancers was 0.20 (95 per cent confidence interval 0.13 to 0.30). In women without prior cancer, all-cause mortality to age 70 years was reduced (hazard ratio 0.23). The risk is greatly reduced but not eliminated. Since the peritoneum is not removed, a risk of primary peritoneal carcinoma remains [11].

In a molecular study of tissue from nine patients, tubal lesions proved to be precursors of high-grade serous ovarian carcinomas. Evolutionary analyses indicated a window of approximately seven years between the development of the tubal precursor and the onset of carcinoma, with metastases following rapidly [12]. Because of the very small number of cases, this work describes a biological mechanism, not a time course that can be transferred to the individual case.

7. Assessment

7.1 The classification in May 2017

In May 2017 two types of evidence were available. The absence from population databases corresponded to the criterion PM2 (moderate), and the concordant splice prediction to the criterion PP3 (supporting). Under the combining rules of the standard, this combination is not sufficient for a classification as likely pathogenic [3]. Variants at position +5 are not canonical splice site variants, and PVS1 was not applicable on the basis of a mere prediction [3, 4]. The classification as class 3 corresponded to the rules in force at the time.

The claimant contends that the defendant should have arranged an RNA analysis in 2017. Such analyses were available in specialised laboratories but, in the undersigned's experience, were not a regular part of diagnostic reporting. The standard required efforts to resolve uncertain variants without prescribing a particular method [3]. The undersigned regards this as an unused opportunity, not as a departure from an established standard.

The report was professionally incomplete insofar as the note on possible changes in the classification and the recommendation to make a later enquiry were missing. Both were contained in international recommendations in 2017 [2, 3]. Whether this is legally significant is for the Chamber to assess.

The clinical recommendations of 2017 corresponded to the standard. An uncertain variant should not be used for clinical decision-making [3], and intensified surveillance based on the family history was consistent [2]. The decision not to perform a salpingo-oophorectomy is supported by the consensus recommendations, which link the procedure to a pathogenic variant [9]. In the data set of Mersch et al., the majority of uncertain variants remained unchanged, and those reclassified were overwhelmingly downgraded [7].

7.2 Evidence and formal classifications up to 2025

Point in time	Available evidence or event (fact of the case)	Criteria	Formal classification at that time
May 2017	Absence from population databases, splice prediction	PM2, PP3	Class 3 (defendant)
October 2020	RNA data public: exon loss, frameshift, no normal transcript from the variant allele	PM2 and strong functional evidence (then PS3)	likely pathogenic (university laboratory)
18 March 2021	Reassessment by the defendant on the basis of these RNA data	as October 2020	Class 4 (defendant, internal)
March and April 2024	Tumour findings of the claimant	additional evidence under gene-specific rules	Class 5 (university hospital, internal laboratory classification, 26 April 2024)
May 2025	Assessment by the expert panel	ENIGMA specification	pathogenic (ClinGen ENIGMA expert panel)

Complete exon loss with a frameshift and no normal transcript from the variant allele demonstrates loss of function. Under the 2015 rules this was to be classed as strong functional evidence (PS3), and together with PM2 the combining rules of 2015 result in a classification as likely pathogenic [3]. Today the same finding is captured with RNA-based PVS1 [5]. The undersigned shares the defendant's class 4 assessment for the state of knowledge at that time.

Class 4 was therefore justifiable at the earliest from October 2020, when the RNA data became public, and formally existed at the defendant from 18 March 2021.

A formal classification as class 5 did not exist before 26 April 2024, and the undersigned does not make a retrospective class 5 classification. Whether the evidence in April 2024 reached the threshold for class 5 under the gene-specific rules cannot be examined without a listing of criteria. The panel

classification of May 2025 confirms the direction but does not establish any earlier class 5 classification. For the questions put by the court the distinction is not decisive, because class 4 and class 5 trigger the same preventive recommendations [2].

7.3 Reassessment and communication from a medical and professional point of view

The recommendations set out in section 6.3 [2, 3, 8] and the recall system relating to the centres of the Consortium [9] do not establish a professional standard for the communication of reclassifications in the period 2017 to 2024 that was binding on all laboratories in Germany.

The communication pathway runs from the laboratory to the referring physician, here Dr B. [fictitious], and from her to the patient [3, 8]. The defendant's operating procedure provided for written information of the referring physician. This did not take place, so that the information could not reach the claimant by this route.

The upgrade from class 3 to class 4 was clinically significant because it changed the preventive recommendations [2, 9], and it belongs to the reclassifications whose communication the ACMG statement prioritises [8]. From a medical and professional point of view, the reassessment of March 2021 should have led to an updated report to the referring physician, as the defendant's operating procedure provided.

The following questions remain open and are for the Chamber to decide: whether a legal duty of the defendant to communicate to the referring physician arose from the professional recommendations, the operating procedure or § 11 GenDG, whether such a duty would also have existed without the operating procedure, whether there was in addition a duty to inform the claimant, and how the migration error is to be assessed.

7.4 Hypothetical course had the information been available in time

If, contrary to the assessment in section 7.1, a classification as class 4 or 5 is assumed as early as 2017, salpingo-oophorectomy would have been recommended to the claimant on reaching the age of 40 in January 2018. The consensus recommendations describe the option from 35 years as a lowered age limit only in 2021 [9]. In addition there would have been counselling on risk-reducing mastectomy [9] and the offer of predictive testing to relatives [2].

On communication in spring 2021 the claimant was 43 years old. The recommendation for salpingo-oophorectomy would have applied immediately [9]. It is assumed that a few months would have passed between communication to the referring physician, information of the claimant, counselling and surgery, that is, surgery in approximately the second half of 2021, around two and a half years before diagnosis. Whether and when the claimant would have undergone surgery is for the Chamber to determine. Medically, completed family planning, family history and age spoke in favour, and against it mainly the consequences of premature menopause.

7.5 Causation for the ovarian cancer

Three levels must be distinguished.

Population-level effect. In the cohorts, after the procedure and relative to the time at risk, approximately one fifth as many ovarian, fallopian tube and peritoneal cancers occurred as without the procedure [10, 11]. These are observational data that do not distinguish according to how long before a later diagnosis surgery was performed.

Individual counterfactual outcome. Whether precisely the carcinoma that occurred in the claimant would have been avoided cannot be read from a hazard ratio. It depends on whether an occult carcinoma or dissemination was already present at the time of surgery and whether the tumour

originated in the adnexa or primarily in the peritoneum. This cannot be determined retrospectively. The study of nine patients [12] supports only the general assumption that years may lie between precursor and carcinoma, and says nothing about the stage in the claimant in 2018 or 2021.

Remaining risk of peritoneal carcinoma. Even after a complete procedure, a risk of primary peritoneal carcinoma remains [11]. A statement bordering on certainty is therefore not possible in any scenario.

Surgery at the beginning of 2018. Six years would have passed until diagnosis. The long interval tends to speak against an invasive carcinoma having already been present in 2018, but this cannot be ruled out. Surgery at the beginning of 2018 would, according to the cohort data, have markedly reduced the claimant's risk of carcinoma of the ovaries, fallopian tubes and peritoneum. Whether it would have prevented precisely this specific tumour cannot be reliably determined. Patient-related data on the time of tumour development and on the tissue of origin are lacking for this, and the cohort values cannot be converted into an individual probability. The undersigned therefore does not give a grade for individual avoidance. Medically, the earlier date merely indicates that the prospect of avoidance would have been greater in 2018 than with surgery in 2021.

Surgery in the second half of 2021. Approximately two and a half years would have passed until diagnosis. Three constellations are conceivable: only a precursor, which would have been removed with the fallopian tubes, an occult early carcinoma, which would have been detected histologically at an earlier stage, or dissemination already present. There are no reliable data for weighting them in an individual patient. The undersigned considers a more favourable course, that is, avoidance or earlier detection, to be possible and plausible, but it cannot be soundly established that this is more likely than not. Whether earlier detection would have improved the prognosis would have to be assessed from a gynaecological oncology perspective.

7.6 Alternative explanations and limits of the assessment

Ovarian cancer can also develop independently of the variant. The indication of loss of the wild-type allele and the HRD in the tumour are well compatible with *BRCA1*-related tumour development. A misidentification or sample mix-up is very unlikely, since two laboratories independently detected the variant in the germline and a third detected it in the tumour.

The statements in section 7.5 are based on group data from cohorts recruited predominantly through counselling centres [1, 11] and do not represent an individual value for the claimant.

7.7 Breast cancer surveillance

At the centres of the Consortium, intensified surveillance is open to carriers of pathogenic *BRCA1* variants as well as to women with an increased familial risk [9]. Had a class 4 variant been known, it would, in the undersigned's assessment, not have looked substantially different. A reduction of breast cancer risk through salpingo-oophorectomy in *BRCA1* is not established according to the consensus recommendations [9]. The opportunity to consider risk-reducing mastectomy earlier was missing. Since no breast cancer has occurred, no ascertainable health disadvantage follows from this. The option remains available [9].

8. Answers to the questions put by the court

Question 1: Did the classification as class 3 in the report of 22 May 2017 correspond to the professional standard at that time?

Answer: Yes. With the evidence available at the time (PM2, PP3), only class 3 was possible under the ACMG/AMP standard. The missing note on possible changes and later enquiry was professionally incomplete.

Question 2: From what point in time did the knowledge support an upgrade?

Answer: Class 4 was justifiable at the earliest from October 2020 with the public RNA data and formally existed at the defendant from 18 March 2021. A formal class 5 classification first existed on 26 April 2024 (university hospital), and the panel classification followed in May 2025. For the preventive recommendations, the difference between class 4 and class 5 is of no significance.

Question 3: What requirements applied to reassessment and communication?

Answer: Continuous review of all variants was not generally recommended. What was recommended was a note in the initial report and periodic enquiry, and since 2019 additionally the priority communication of clinically relevant upgrades to the referring physician, through whom the patient is informed. The defendant's operating procedure expressly provided for this. From a medical and professional point of view, the reassessment of March 2021 should have led to an updated report to the referring physician. A German standard binding on all laboratories cannot be demonstrated. Which legal duties existed is for the Chamber to decide.

Question 4: What measures would have been recommended had the information been known in 2017 or in 2021 respectively?

Answer: In both cases risk-reducing salpingo-oophorectomy, with knowledge in 2017 at 40 years from January 2018, with knowledge in 2021 immediately. For 2021, surgery in approximately the second half of the year is taken as the basis, which is an assumption about the timing. In addition there would have been counselling on risk-reducing mastectomy and predictive testing of relatives. Breast cancer surveillance would have remained essentially unchanged.

Question 5: With what probability would the ovarian cancer have been avoided or detected earlier?

Answer: The risk reduction of approximately 80 per cent is a group effect, not an individual probability of avoidance. Surgery at the beginning of 2018 would have markedly reduced the risk. Whether it would have prevented precisely this tumour cannot be reliably determined, and an individual probability cannot be derived from the cohort data. A residual risk of peritoneal carcinoma remains in any case. With surgery in 2021, avoidance or earlier detection is possible, and the prospect of this would have been lower than in 2018. The final assessment of causation and the question of whether the claimant would have consented are matters for the Chamber.

Question 6: Are there further health disadvantages, in particular with regard to breast cancer surveillance?

Answer: As far as can be ascertained, no. Surveillance would not have been substantially different, and no breast cancer has occurred. Risk-reducing mastectomy remains an option.

9. Summary

Key findings

- The classification of the hypothetical *BRCA1* variant as uncertain in May 2017 corresponded to the standard at that time. The report should, however, have pointed out possible changes in the classification.
- With publicly available RNA data, an upgrade to class 4 was justifiable from October 2020. The defendant made it on 18 March 2021, and no updated report was issued to the referring physician. A formal class 5 classification existed only in April 2024.
- Professional recommendations and the operating procedure provided for communication to the referring physician. Which legal duties followed is for the Chamber to decide.
- The risk reduction of approximately 80 per cent is a cohort effect. Surgery in 2018 would have markedly reduced the risk. Whether it would have prevented this specific tumour cannot be reliably determined. For surgery in 2021, a more favourable course is possible.

The 2017 classification corresponded to the knowledge of its time. What is in dispute is the period from March 2021, during which the laboratory had implemented new evidence internally, but the information reached neither the referring physician nor the claimant. Equally central is the distinction between the group effect of a preventive measure and the individual case.

8 November 2026

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